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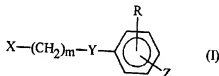
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(54) **Benzimidazole derivatives, their preparation and their therapeutic use**

(57) Compounds of formula (I):



[in which: X represents an optionally substituted benzimidazole group; Y represents an oxygen or sulphur atom; Z represents a 2,4-dioxothiazolidin-5-ylidenemethyl, 2,4-dioxothiazolidin-5-ylmethyl, 2,4-dioxo-oxazolidin-5-ylmethyl, 3,5-dioxooxazolidin-2-ylmethyl or N-hydroxyureidomethyl group; R represents hydrogen, alkyl, alkoxy, halogen, hydroxy, nitro, amino or aralkyl; and m is an integer from 1 to 5] have valuable activity for the treatment and/or prophylaxis of a variety of disorders, including one or more of: hyperlipemia, hyperglycemia, obesity, impaired glucose tolerance (IGT), insulin resistance and diabetic complications.

Description

The present invention relates to a series of benzimidazole compounds having hypoglycaemic, anti-diabetic, anti-cataract and 5-lipoxygenase inhibitory activities, the ability to inhibit the formation of lipid peroxide and related activities, as described in more detail hereafter, and provides processes for their preparation and methods and compositions for their use.

Insulin and sulphonylurea compounds, including tolbutamide and glipizide, have been used for the treatment of diabetes mellitus and hyperglycaemia. More recently, it has been discovered that compounds which, like those of the present invention, contain, *inter alia*, a thiazolidinedione, oxazolidinedione or related group attached, via a methylene or methylidene group, to a benzene ring have this type of activity, and have been proposed for the treatment of non-insulin-dependent diabetes mellitus.

(1) Many thiazolidine derivatives have been reported to have hypoglycaemic activity, for example those described in: European Patent Publication No. 008203; European Patent Publication No. 139421; Chem. Pharm. Bull. 30, 3580-3600 (1982) by Y. Kawamatsu *et al.*; and in European Patent Publication No. 0441605.

(2) Compounds containing heterocyclic ring groups are disclosed in, for example: European Patent Publication No. 208420; European Patent Publication No. 528734; WO 92/07550A; WO 92/07839A; European Patent Publication No. 177353; European Patent Publication No. 306228; and European Patent Publication No. 356214.

(3) Oxazolidine-2,4-dione compounds having hypoglycaemic activity are disclosed in, for example: WO 91/07107A; and WO 92/02520A.

(4) In addition, compounds containing an N-hydroxyureido group or a 3,5-dioxooxadiazolidin-2-ylmethyl/phenyl group and having this type of activity are disclosed in WO 92/03425A.

However, these compounds have a number of disadvantages, for example, their activity is inadequate or there are problems with their safety. Stronger and safer preventive and/or therapeutic agents for these diseases are therefore desired in practice.

The relationship between thiazolidine derivatives and various diseases is described in the following literature:

The effect of thiazolidine compounds on hyperglycaemia has been reported in Diabetes 32(9), 804-810 (1983); Diabetes 37(11), 1549-1558 (1988); Prog. Clin. Biol. Res. 265, 177-192 (1988); Metabolism 37(3), 276-280 (1988); Arzneimittelforschung 40(1), 37-42 (1990); Arzneimittelforschung 40(2 Pt 1), 156-162 (1990); and Arzneimittelforschung 40(3), 263-267 (1990).

The effect of thiazolidine compounds on hyperlipidaemia has been reported in Diabetes 40(12), 1669-1674 (1991); Am. J. Physiol. 267(1 Pt 1), E95-E101 (1994); and Diabetes 43(10), 1203-1210 (1994).

The effect of thiazolidine compounds on impaired glucose tolerance and insulin resistance has been reported in Arzneimittelforschung 40(2 Pt 1), 156-162 (1990); Metabolism 40(10), 1025-1230 (1991); Diabetes 43(2), 204-211 (1994); and N. Engl. J. Med. 331(18), 1226-1227 (1994).

The effect of thiazolidine compounds on hypertension has been reported in Metabolism 42(1), 75-80 (1993); Am. J. Physiol. 265 (4 Pt 2), R726-R732 (1993); and Diabetes 43(2), 204-211 (1994).

The effect of thiazolidine compounds on cachexia has been reported in Endocrinology 135(5), 2279-2282 (1994); and Endocrinology 135(4), 1474-1481 (1995).

The effect of thiazolidine compounds on nephropathy has been reported in the Journal of Japan Diabetes Society 38, Extra number (1995).

The effect of thiazolidine compounds on coronary artery diseases has been reported in Am. J. Physiol. 265(4 Pt 2), R726-R732 (1993); and Hypertension 24(2), 170-175 (1994).

The effect of thiazolidine compounds on arteriosclerosis has been reported in Am. J. Physiol. 265(4 Pt 2), R726-R732 (1993).

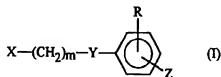
In addition, a high risk of diabetic occurrence has recently been reported in normal persons who have insulin resistance which is not accompanied by impaired glucose tolerance [in other words, insulin resistant non-IGT (NGT)] in N. Engl. J. Med. 331(18), 1226-1227 (1994). This fact suggests that an agent which can improve insulin resistance may be useful for the prevention of such diabetic occurrence in normal persons.

We have now discovered that the inclusion in such compounds of certain specific bicyclic nitrogen-containing ring systems results in compounds of much improved activity.

In accordance with the present invention, we have discovered a series of new chemical compounds which contain a benzimidazole ring and which may be regarded as thiazolidine and oxazolidine derivatives or as ring-opened derivatives thereof, at least some of which may be useful for the treatment and/or prophylaxis of a variety of disorders,

including one or more of: hyperlipaemia, hyperglycaemia, obesity, impaired glucose tolerance (IGT), insulin resistance and diabetic complications, in mammals, including human beings.

Thus, the present invention provides compounds of formula (I) :

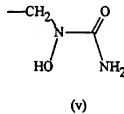
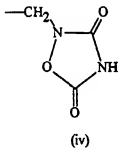
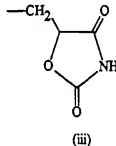
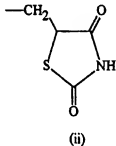
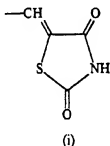


In which:

X represents a benzimidazole group which is unsubstituted or is substituted by at least one of substituents α , defined below;

Y represents an oxygen atom or a sulphur atom;

Z represents a group of formula (i), (ii), (iii), (iv) or (v) :



R represents:

- a hydrogen atom;
- an alkyl group having from 1 to 4 carbon atoms;
- an alkoxy group having from 1 to 4 carbon atoms;
- a halogen atom;
- a hydroxy group;
- a nitro group;
- a group of formula $-NR^aR^b$,

in which R^a and R^b are the same or different and each represents a hydrogen atom, an alkyl group having from 1 to 8 carbon atoms, an aralkyl group in which an alkyl group having from 1 to 5 carbon atoms is substituted

by a carbocyclic aryl group having from 6 to 10 carbon atoms; a carbocyclic aryl group having from 6 to 10 carbon atoms; an aliphatic acyl group having from 1 to 11 carbon atoms; an aryl-aliphatic acyl group in which an aliphatic acyl group having from 2 to 6 carbon atoms is substituted by at least one carbocyclic aryl group having from 6 to 10 carbon atoms; or an aromatic acyl group having from 7 to 11 carbon atoms; or an aralkyl group in which an alkyl group having from 1 to 5 carbon atoms is substituted by a carbocyclic aryl group having from 6 to 10 carbon atoms; and

m represents an integer from 1 to 5;

said substituents α are selected from:

an alkyl group having from 1 to 4 carbon atoms;
 an alkoxy group having from 1 to 4 carbon atoms;
 a benzyloxy group;
 a halogen atom;
 a hydroxy group;
 an acetoxy group;
 a phenylthio group;
 an alkylthio group having from 1 to 4 carbon atoms;
 a trifluoromethyl group;
 a nitro group;
 a group of formula $-NR^aR^b$, in which R^a and R^b are as defined above;
 a carbocyclic aryl group having from 6 to 10 carbon atoms which is unsubstituted or is substituted by at least one of substituents β , defined below; or an aralkyl group in which an alkyl group having from 1 to 5 carbon atoms is substituted by a carbocyclic aryl group which has from 6 to 10 carbon atoms and which is unsubstituted or is substituted by at least one of substituents β , defined below;

said substituents β are selected from alkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, halogen atoms, hydroxy groups, nitro groups, phenyl groups, trifluoromethyl groups and groups of formula $-NR^aR^b$, in which R^a and R^b are as defined above; and salts thereof.

The invention also provides a pharmaceutical composition for the treatment or prophylaxis of insulin resistance, diabetes, hyperglycaemia, arteriosclerosis, cataracts, hyperlipaemia, obesity, impaired glucose tolerance, hypertension, polycystic ovary syndrome, gestational diabetes mellitus or insulin resistant non-HGT, cataracts and complications thereof, which composition comprises an effective amount of an active compound in admixture with a pharmaceutically acceptable carrier or diluent, in which said active compound is selected from compounds of formula (I), defined above, and salts thereof.

The invention still further provides the use of compounds of formula (I), defined above, and salts thereof for the manufacture of a medicament for the treatment or prophylaxis of insulin resistance, diabetes, hyperglycaemia, arteriosclerosis, hyperlipaemia, obesity, impaired glucose tolerance, hypertension, polycystic ovary syndrome, gestational diabetes mellitus or insulin resistant non-HGT, cataracts and complications thereof.

The invention also provides a pharmaceutical composition for the inhibition of aldose reductase, 5-lipoxygenase or lipid peroxide, and complications thereof, which composition comprises an effective amount of an active compound in admixture with a pharmaceutically acceptable carrier or diluent, in which said active compound is selected from compounds of formula (I), defined above, and salts thereof.

The invention still further provides the use of compounds of formula (I), defined above, and salts thereof for the manufacture of a medicament for the inhibition of aldose reductase, 5-lipoxygenase or lipid peroxide, and complications thereof.

The invention also provides processes for the preparation of the compounds of the present invention, which processes are described in more detail hereafter.

Where X represents an unsubstituted benzimidazole group, this may be, for example, a 1-benzimidazolyl, 2-benzimidazolyl, 4-benzimidazolyl, 5-benzimidazolyl, 6-benzimidazolyl or 7-benzimidazolyl group.

Alternatively, X may represent a substituted benzimidazole group, in which case, the substituent is one or more of substituents α , defined above and exemplified below. There is no restriction on the number of substituents on the group other than that imposed by the number of substitutable positions, i.e. 5. Hence, the possible number of substituents is from 1 to 5. More preferably, in the case of those compounds intended for the treatment or prophylaxis of hyperglycaemia, there are from 1 to 3 such substituents, one substituent being most preferred. In the case of those compounds intended for the inhibition of lipid peroxide, we most prefer those compounds having five substituents.

Where any of R, substituent α and/or substituent β represents an alkyl group, this may be a straight or branched chain alkyl group having from 1 to 4 carbon atoms. Examples of such alkyl groups include the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and t-butyl groups, of which we prefer the methyl group.

Where any of R, substituent α and/or substituent β represents an alkoxy group, this may be a straight or branched chain alkoxy group having from 1 to 4 carbon atoms. Examples of the such alkoxy groups include the methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy and t-butoxy groups, of which we prefer the methoxy group.

Where any of R, substituent α and/or substituent β represents a halogen atom, this may be, for example, a bromine, chlorine or fluorine atom, of which the fluorine atom is preferred.

Where any of R, substituent α , R^a and/or R^b represents an aralkyl group, this may be as defined above, i.e. it is an alkyl group having from 1 to 5 carbon atoms which is substituted by at least one carbocyclic aryl group having from 6 to 10 ring carbon atoms. In the case of R, R^a and R^b, the aryl group is preferably not substituted. In the case of substituents α , the group may be substituted or unsubstituted, although it is preferably unsubstituted. Although there may be from 1 to 3 aryl groups as substituents on the alkyl part, there is preferably only one such aryl group. The total number of carbon atoms in the alkyl part and the carbocyclic ring of the aryl part is preferably from 7 to 11. The alkyl part of the aralkyl group may be a straight or branched chain alkyl group having from 1 to 5 carbon atoms. Examples of such unsubstituted aralkyl groups include the benzyl, 2-phenylethyl, 1-phenylethyl, 3-phenylpropyl, 2-phenylpropyl, 1-phenylpropyl, 4-phenylbutyl, 1-phenylbutyl, 5-phenylpentyl, 1-naphthylmethyl and 2-naphthylmethyl groups, of which the benzyl group is preferred.

Where any of R, substituent α and/or substituent β represents a group of formula $-NR^aR^b$, this is an amino group which is unsubstituted or may optionally be substituted by any of the groups defined for R^a and R^b other than a hydrogen atom. Examples of such groups include:

(1) Alkyl groups which may be straight or branched chain groups having from 1 to 8 carbon atoms, for example the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, t-butyl, pentyl, 1-methylbutyl, 1-ethylpropyl, 2-methylbutyl, 3-methylbutyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 2,2-dimethylpropyl, hexyl, 1-methylpentyl, 1-ethylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, heptyl, 1-methylhexyl, 1-ethylpentyl, 1-propylbutyl, 3,3-dimethylpentyl, octyl, 1-methylheptyl, 2-ethylhexyl and 1,1,3,3-tetramethylbutyl groups, of which we prefer those straight or branched chain alkyl groups having from 1 to 6 carbon atoms, and most prefer those straight or branched chain alkyl groups having from 1 to 4 carbon atoms, particularly the methyl and ethyl groups.

(2) Aralkyl groups preferably having a total of from 7 to 11 carbon atoms in the alkyl group and the aromatic carbocyclic ring, which may be as defined and exemplified above in relation to substituents α .

(3) Aryl groups having from 6 to 10 carbon atoms, and preferably 6 or 10 carbon atoms, in an aromatic carbocyclic ring. Such a group may be substituted or unsubstituted and, if substituted, is preferably substituted by one or more of substituents β , defined above and exemplified below. It is, however, preferably unsubstituted. Examples of such aryl groups include the phenyl, 1-naphthyl and 2-naphthyl groups.

(4) Aliphatic acyl groups which may be straight or branched chain groups having from 1 to 11 carbon atoms, for example, the formyl, acetyl, propionyl, butyryl, isobutyryl, pivaloyl, valeryl, isovaleryl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl and undecanoyl groups, of which we prefer the formyl, acetyl, propionyl, butyryl, isobutyryl, pivaloyl, valeryl and hexanoyl groups.

(5) Aryl-aliphatic acyl groups in which an aliphatic acyl group having from 2 to 6 carbon atoms is substituted by at least one carbocyclic aryl group having from 6 to 10 carbon atoms. The aryl group may be as defined and exemplified in (3) above. There may be from 1 to 3 such aryl substituents, preferably one. Examples of such aryl-aliphatic acyl groups include the phenylacetyl, 3-phenylpropionyl, 4-phenylbutyryl, 5-phenylpentanoyl, 6-phenylhexanoyl, α -methylphenylacetyl and α,α -dimethylphenylacetyl groups, of which the phenylacetyl group is preferred.

(6) Aromatic acyl groups having from 7 to 11 carbon atoms, in which the aromatic part is a carbocyclic aryl group which may be as defined and exemplified in (3) above, for example, the benzoyl, 1-naphthoyl and 2-naphthoyl groups, of which the benzoyl group is preferred.

The groups R^a and R^b may be the same or different. If they are the same and both represent hydrogen atoms, the group is a simple unsubstituted amino group. Alternatively, one may be a hydrogen atom and the other may be one of the other groups defined and exemplified above, or one may be one of the groups other than hydrogen defined and

exemplified above and the other may be another of the groups other than hydrogen defined and exemplified above, or they may be the same and both may be one of the groups other than hydrogen defined and exemplified above. In general, we prefer that both should be hydrogen atoms or that one should be a hydrogen atom and the other should be one of the other groups defined and exemplified above.

Accordingly, where R, substituent α and/or substituent β represents an amino group, preferred examples of such amino groups include:

(1) amino groups having a single alkyl substituent, i.e. R^a represents a hydrogen atom and R^b represents an alkyl group, for example the methylamino, ethylamino, propylamino, isopropylamino, butylamino, isobutylamino, sec-butylamino, 1-butylamino, pentylamino, 1-methylbutylamino, 1-ethylpropylamino, 2-methylbutylamino, 3-methylbutylamino, 1,1-dimethylpropylamino, 1,2-dimethylpropylamino, 2,2-dimethylpropylamino, hexylamino, 1-methylpentylamino, 1-ethylbutylamino, 2-methylpentylamino, 3-methylpentylamino, 4-methylpentylamino, 1,1-dimethylbutylamino, 1,2-dimethylbutylamino, 1,3-dimethylbutylamino, 2,2-dimethylbutylamino, 2,3-dimethylbutylamino, 3,3-dimethylbutylamino, 1,1,2-trimethylpropylamino, 1,2,2-trimethylpropylamino, heptylamino, 1-methylhexylamino, 1-ethylpentylamino, 1-propylbutylamino, 3,3-dimethylpentylamino, octylamino, 1-methylheptylamino, 2-ethylhexylamino and 1,1,3,3-tetramethylbutylamino groups;

(2) amino groups having a single aralkyl substituent, i.e. R^a represents a hydrogen atom and R^b represents an aralkyl group, for example the benzylamino, 2-phenylethylamino, 1-phenylethylamino, 3-phenylpropylamino, 2-phenylpropylamino, 1-phenylpropylamino, 4-phenylbutylamino, 1-phenylbutylamino, 5-phenylpentylamino, 1-naphthylmethylamino and 2-naphthylmethylamino groups;

(3) amino groups having a single aryl substituent, i.e. R^a represents a hydrogen atom and R^b represents an aryl group, for example the phenylamino, 1-naphthylamino and 2-naphthylamino groups;

(4) amino groups having a single aliphatic acyl substituent, i.e. R^a represents a hydrogen atom and R^b represents an aliphatic acyl group, for example the formylamino, acetylamino, propionylamino, butylamino, isobutyrylamino, pivaloylamino, pentanoylamino, hexanoylamino, heptanoylamino, octanoylamino, nonanoylamino, decanoylamino and undecanoylamino groups;

(5) amino groups having a single aryl-aliphatic acyl substituent, i.e. R^a represents a hydrogen atom and R^b represents an aryl-aliphatic acyl group, for example the phenylacetylaminio, 3-phenylpropionylamino, 4-phenylbutyrylamino, 5-phenylpentanoylamino, 6-phenylhexanoylamino, α -methylphenylacetylaminio and α , α -dimethylphenylacetylaminio groups;

(6) amino groups having a single aromatic acyl substituent, i.e. R^a represents a hydrogen atom and R^b represents an aromatic acyl group, for example the benzoylamino, 1-naphthoylamino and 2-naphthoylamino groups;

(7) amino groups having two alkyl substituents, i.e. R^a and R^b both represent alkyl groups which may be the same or different, for example the dimethylamino, diethylamino, N-methyl-N-ethylamino and N-methyl-N-pentylamino groups;

(8) amino groups having a single alkyl substituent and a single aralkyl substituent, i.e. R^a represents an alkyl group and R^b represents an aralkyl group, for example the N-ethyl-N-benzylamino, N-t-butyl-N-benzylamino and N-hexyl-N-benzylamino groups;

(9) amino groups having a single alkyl substituent and a single aryl substituent, i.e. R^a represents an alkyl group and R^b represents an aryl group, for example the N-methyl-N-phenylamino, N-ethyl-N-phenylamino and N-octyl-N-phenylamino groups;

(10) amino groups having a single alkyl substituent and a single aliphatic acyl substituent, i.e. R^a represents an alkyl group and R^b represents an aliphatic acyl group, for example the N-propyl-N-acetylaminio, N-pentyl-N-propionylamino and N-ethyl-N-hexanoylamino groups;

(11) amino groups having a single alkyl substituent and a single aryl-aliphatic acyl substituent, i.e. R^a represents an alkyl group and R^b represents an aryl-aliphatic acyl group, for example the N-ethyl-N-phenylacetylaminio, N-isopropyl-N-(2-phenylpropionyl)amino and N-methyl-N-(6-phenylhexanoyl)-amino groups;

(12) amino groups having a single alkyl substituent and a single aromatic acyl substituent, i.e. R^a represents an alkyl group and R^b represents an aromatic acyl group, for example the N-methyl-N-benzoylamino, N-sec-butyl-N-benzoylamino and N-heptyl-N-benzoylamino groups;

(13) amino groups having two aralkyl substituents, i.e. R^a and R^b both represent aralkyl groups which may be the same or different, for example the dibenzylamino, N-benzyl-N-(3-phenylpropyl)amino and N-benzyl-N-(2-naphthylmethyl)amino groups;

(14) amino groups having a single aralkyl substituent and a single aryl substituent, i.e. R^a represents an aralkyl group and R^b represents an aryl group, for example the N-benzyl-N-phenylamino and N-(3-phenylpropyl)-N-phenylamino groups;

(15) amino groups having a single aralkyl substituent and a single aliphatic acyl substituent, i.e. R^a represents an aralkyl group and R^b represents an aliphatic acyl group, for example the N-benzyl-N-acetylamino, N-benzyl-N-propionylamino and N-benzyl-N-pentanoylamino groups;

(16) amino groups having a single aralkyl substituent and a single aryl-aliphatic acyl substituent, i.e. R^a represents an aralkyl group and R^b represents an aryl-aliphatic acyl group, for example the N-benzyl-N-phenylacetylamino and N-benzyl-N-(4-phenylbutyl)amino groups;

(17) amino groups having a single aralkyl substituent and a single aromatic acyl substituent, i.e. R^a represents an aralkyl group and R^b represents an aromatic acyl group, for example the N-benzyl-N-benzoylamino and N-(2-phenylethyl)-N-benzoylamino groups;

(18) amino groups having two aryl substituents, i.e. R^a and R^b both represent aryl groups which may be the same or different, for example the diphenylamino, N-(1-naphthyl)-N-phenylamino and N-(2-naphthyl)-N-phenylamino groups;

(19) amino groups having a single aryl substituent and a single aliphatic acyl substituent, i.e. R^a represents an aryl group and R^b represents an aliphatic acyl group, for example the N-phenyl-N-acetylamino, N-phenyl-N-propionylamino and N-phenyl-N-hexanoylamino groups;

(20) amino groups having a single aryl substituent and a single aryl-aliphatic acyl substituent, i.e. R^a represents an aryl group and R^b represents an aryl-aliphatic acyl group, for example the N-phenyl-N-phenylacetylamino and N-phenyl-N-(4-phenylbutyl)amino groups;

(21) amino groups having a single aryl substituent and a single aromatic acyl substituent, i.e. R^a represents an aryl group and R^b represents an aromatic acyl group, for example the N-phenyl-N-benzoylamino and N-phenyl-N-(2-naphthoyl)amino groups;

(22) amino groups having two aliphatic acyl substituents, i.e. R^a and R^b both represent aliphatic acyl groups which may be the same or different, for example the diacetylamino, N-acetyl-N-propionylamino and N-butyryl-N-hexanoylamino groups;

(23) amino groups having a single aliphatic acyl substituent and a single aryl-aliphatic acyl substituent, i.e. R^a represents an aliphatic acyl group and R^b represents an aryl-aliphatic acyl group, for example the N-acetyl-N-phenylacetylamino, N-acetyl-N-(4-phenylbutyl)amino and N-butyryl-N-phenylacetylamino groups;

(24) amino groups having a single aliphatic acyl substituent and a single aromatic acyl substituent, i.e. R^a represents an aliphatic acyl group and R^b represents an aromatic acyl group, for example the N-acetyl-N-benzoylamino and N-butyryl-N-(2-naphthoyl)amino groups;

(25) amino groups having two aryl-aliphatic acyl substituents, i.e. R^a and R^b both represent aryl-aliphatic acyl groups which may be the same or different, for example the N-N-diphenylacetylamino, N-phenylacetyl-N-(2-phenylpropionyl)amino and N-phenylacetyl-N-(4-phenylbutyl)amino groups;

(26) amino groups having a single aryl-aliphatic acyl substituent and a single aromatic acyl substituent, i.e. R^a represents an aryl-aliphatic acyl group and R^b represents an aromatic acyl group, for example the N-phenylacetyl-

N-benzoylamino and N-phenylacetyl-N-(2-naphthyl)amino groups; and

(27) amino groups having two aromatic acyl substituents, i.e. R^a and R^b both represent aromatic acyl groups which may be the same or different, for example the dibenzoylamino and N-benzoyl-N-(2-naphthyl)amino groups.

Where substituent α represents an alkylthio group, this may be a straight or branched chain alkylthio group having from 1 to 4 carbon atoms, for example the methylthio, ethylthio, propylthio, isopropylthio, butylthio, isobutylthio, sec-butylthio and t-butylthio groups.

Where a substituent α represents an aryl group, this may be a carbocyclic aryl group having from 6 to 10 carbon atoms which is unsubstituted or is substituted by one or more of substituents β . Examples of the unsubstituted aryl groups include the phenyl, 1-naphthyl and 2-naphthyl groups. Where the aryl group is substituted, there is no restriction on the number of substituents, except such as may be imposed by the number of substitutable positions and possibly by steric constraints; thus the maximum number of substituents on a phenyl group is 5, whilst that on a naphthyl group is 7. In general, however, from 1 to 3 substituents are preferred, one substituent generally being more preferred.

Moreover, where substituent β represents an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom or a group of formula $-NR^aR^b$, these may be as defined and exemplified above in relation to the corresponding group or atom represented by substituent α . Alternatively, substituent β may be a hydroxy group, a nitro group, a phenyl group or a trifluoromethyl group.

Examples of substituted aryl groups which may be represented by substituent α include:

(1) Aryl groups substituted by at least one straight or branched chain alkyl group having from 1 to 4 carbon atoms, for example, the 4-methylphenyl, 4-ethylphenyl, 4-propylphenyl, 4-isopropylphenyl, 4-butylphenyl, 4-isobutylphenyl, 4-sec-butylphenyl, 4-t-butylphenyl, 4-methyl-1-naphthyl, 5-ethyl-1-naphthyl, 8-propyl-1-naphthyl, 4-isopropyl-1-naphthyl, 5-butyl-1-naphthyl, 4-isobutyl-1-naphthyl, 4-sec-butyl-1-naphthyl, 4-t-butyl-1-naphthyl, 4-methyl-2-naphthyl, 5-ethyl-2-naphthyl, 8-propyl-2-naphthyl, 4-isopropyl-2-naphthyl, 5-butyl-2-naphthyl, 8-isobutyl-2-naphthyl, 4-sec-butyl-2-naphthyl and 5-t-butyl-2-naphthyl groups.

(2) Aryl groups substituted by at least one straight or branched chain alkoxy group having from 1 to 4 carbon atoms, for example, the 4-methoxyphenyl, 4-ethoxyphenyl, 4-propoxyphenyl, 4-isopropoxyphenyl, 4-butoxyphenyl, 4-isobutoxyphenyl, 4-sec-butoxyphenyl, 4-t-butoxyphenyl, 4-methoxy-1-naphthyl, 5-ethoxy-1-naphthyl, 8-propoxy-1-naphthyl, 4-isopropoxy-1-naphthyl, 5-butoxy-1-naphthyl, 4-isobutoxy-1-naphthyl, 4-sec-butoxy-1-naphthyl, 4-t-butoxy-1-naphthyl, 4-methoxy-2-naphthyl, 5-ethoxy-2-naphthyl, 8-propoxy-2-naphthyl, 4-isopropoxy-2-naphthyl, 5-butoxy-2-naphthyl, 8-isobutoxy-2-naphthyl, 4-sec-butoxy-2-naphthyl and 5-t-butoxy-2-naphthyl groups.

(3) Aryl groups substituted by at least one halogen atom, for example, the 4-bromophenyl, 4-chlorophenyl, 4-fluorophenyl, 4-iodophenyl, 3-chlorophenyl, 3-fluorophenyl, 3-bromophenyl, 3-iodophenyl, 4-bromo-1-naphthyl, 4-chloro-1-naphthyl, 4-fluoro-1-naphthyl, 4-iodo-1-naphthyl, 5-chloro-1-naphthyl, 5-fluoro-1-naphthyl, 5-bromo-1-naphthyl, 8-chloro-1-naphthyl, 4-fluoro-2-naphthyl, 4-bromo-2-naphthyl, 4-chloro-2-naphthyl, 4-iodo-2-naphthyl, 5-bromo-2-naphthyl, 5-chloro-2-naphthyl, 5-fluoro-2-naphthyl and 5-iodo-2-naphthyl groups.

(4) Aryl groups substituted by at least one hydroxy group, for example, the 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 4-hydroxy-1-naphthyl, 5-hydroxy-1-naphthyl, 8-hydroxy-1-naphthyl, 4-hydroxy-2-naphthyl, 5-hydroxy-2-naphthyl and 8-hydroxy-2-naphthyl groups.

(5) Aryl groups substituted by at least one nitro group, for example, the 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 4-nitro-1-naphthyl, 5-nitro-1-naphthyl, 8-nitro-1-naphthyl, 4-nitro-2-naphthyl, 5-nitro-2-naphthyl and 8-nitro-2-naphthyl groups.

(6) Aryl groups substituted by at least one phenyl group, for example, the 3-phenylphenyl, 4-phenylphenyl, 4-phenyl-1-naphthyl, 5-phenyl-1-naphthyl, 8-phenyl-1-naphthyl, 4-phenyl-2-naphthyl, 5-phenyl-2-naphthyl and 8-phenyl-2-naphthyl groups.

(7) Aryl groups substituted by at least one trifluoromethyl group, for example, the 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 4-trifluoromethyl-1-naphthyl, 5-trifluoromethyl-1-naphthyl, 8-trifluoromethyl-1-naphthyl, 4-trifluoromethyl-2-naphthyl, 5-trifluoromethyl-2-naphthyl and 8-trifluoromethyl-2-naphthyl groups.

(8) Aryl groups substituted by at least one unsubstituted amino group, i.e. by a group of formula $-NR^aR^b$, where R^a and R^b both represent hydrogen atoms, for example, the 2-aminophenyl, 3-aminophenyl, 4-ami-

no-1-naphthyl and 8-amino-2-naphthyl

(9) Aryl groups substituted by at least one substituted amino group, examples of which include:

- 5 (i) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an alkyl group, for example, the 3-methylaminophenyl, 4-ethylaminophenyl, 3-propylaminophenyl, 3-isopropylaminophenyl, 4-butylaminophenyl and 3-isobutylaminophenyl groups;
- 10 (ii) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aralkyl group, for example, the 4-benzylaminophenyl, 4-(2-phenylethylamino)phenyl, 4-(1-phenylethylamino)phenyl, 4-(4-phenylbutylamino)phenyl and 4-(1-naphthylmethylamino)phenyl groups;
- 15 (iii) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aryl group, for example, the 4-phenylaminophenyl and 4-(1-naphthylamino)phenyl groups;
- 20 (iv) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aliphatic acyl group, for example, the 4-formylaminophenyl, 4-acetylaminophenyl, 4-butyrylamino-phenyl, 4-pivaloylamino, 4-hexanoylamino, 4-octanoylamino and 4-undecanoylamino groups;
- 25 (v) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aryl-aliphatic acyl group, for example, the 4-phenylacetylaminophenyl, 4-(4-phenylbutylamino)phenyl, 4-(6-phenylhexanoylamino)phenyl, 4-(α -methylphenylacetylaminophenyl and 4-(α , α -dimethylphenylacetylaminophenyl groups;
- 30 (vi) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aromatic acyl group, for example, the 4-benzoylamino, 4-(1-naphthoylamino)phenyl and 4-(2-naphthoylamino)phenyl groups;
- 35 (vii) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a and R^b both represent alkyl groups which may be the same or different, for example, the 4-dimethylaminophenyl, 4-diethylaminophenyl and 4-(N-methyl-N-ethylamino)phenyl groups;
- 40 (viii) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aralkyl group, for example, the 4-(N-ethyl-N-benzylamino)phenyl, 4-(N-t-butyl-N-benzylamino)phenyl and 4-(N-hexyl-N-benzylamino)phenyl groups;
- 45 (ix) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aryl group, for example, the 4-(N-methyl-N-phenylamino)phenyl and 4-(N-octyl-N-phenylamino)phenyl groups;
- 50 (x) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aliphatic acyl group, for example, the 4-(N-propyl-N-acetylaminophenyl and 4-(N-ethyl-N-hexanoylamino)phenyl groups;
- 55 (xi) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N-ethyl-N-phenylacetylaminophenyl and 4-(N-methyl-N-(6-phenylhexanoyl)amino)phenyl groups;
- 60 (xii) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aromatic acyl group, for example, the 4-(N-methyl-N-benzoylamino)phenyl and 4-(N-heptyl-N-benzoylamino)phenyl groups;
- 65 (xiii) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a and R^b both represent aralkyl groups which may be the same or different, for example, the 4-dibenzylaminophenyl and 4-(N-benzyl-N-(2-naphthylmethyl)-amino)phenyl groups;
- (xiv) aryl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an aralkyl group and R^b

represents an aryl group, for example, the 4-(N-benzyl-N-phenylamino)phenyl and 4-(N-(3-phenylpropyl)-N-phenylamino)phenyl groups;

(xv) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aralkyl group and R^b represents an aliphatic acyl group, for example, the 4-(N-benzyl-N-acetylaminophenyl and 4-(N-benzyl-N-pentanoylamino)-phenyl groups;

(xvi) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aralkyl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N-benzyl-N-phenylacetylaminophenyl and 4-(N-benzyl-N-(4-phenylbutyl)amino)phenyl groups;

(xvii) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aralkyl group and R^b represents an aromatic acyl group, for example, the 4-(N-benzyl-N-benzoylamino)phenyl and 4-(N-(2-phenylethyl)-N-benzoylamino)phenyl groups;

(xviii) aryl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aryl groups which may be the same or different, for example, the 4-(diphenylamino)phenyl and 4-(N-(2-naphthyl)-N-phenylamino)phenyl groups;

(xix) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl group and R^b represents an aliphatic acyl group, for example, the 4-(N-phenyl-N-acetylaminophenyl and 4-(N-phenyl-N-hexanoylamino)phenyl groups;

(xx) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N-phenyl-N-phenylacetylaminophenyl and 4-(N-phenyl-N-(4-phenylbutyl)amino)phenyl groups;

(xxi) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl group and R^b represents an aromatic acyl group, for example, the 4-(N-phenyl-N-benzoylamino)phenyl group;

(xxii) aryl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aliphatic acyl groups which may be the same or different, for example, the 4-diacetylaminophenyl and 4-(N-butyl-N-hexanoylamino)phenyl groups;

(xxiii) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aliphatic acyl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N-acetyl-N-phenylacetylaminophenyl and 4-(N-butyl-N-phenylacetylaminophenyl groups;

(xxiv) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aliphatic acyl group and R^b represents an aromatic acyl group, for example, the 4-(N-acetyl-N-benzoylamino)phenyl and 4-(N-butyl-N-(2-naphthoyl)-amino)phenyl groups;

(xxv) aryl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aryl-aliphatic acyl groups which may be the same or different, for example, the 4-(N,N-diphenylacetylaminophenyl and 4-(N-phenylacetyl-N-(4-phenylbutyl)amino)phenyl groups;

(xxvi) aryl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl-aliphatic acyl group and R^b represents an aromatic acyl group, for example, the 4-(N-phenylacetyl-N-benzoylamino)phenyl and 4-(N-phenylacetyl-N-(2-naphthoyl)amino)phenyl groups;

(xxvii) aryl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aromatic acyl groups which may be the same or different, for example, the 4-dibenzoylamino)phenyl and 4-(N-benzoyl-N-(2-naphthoyl)amino)-phenyl groups.

Where substituent α represents an aralkyl group, this is an alkyl group having from 1 to 5 carbon atoms which is substituted by a carbocyclic aryl group having from 6 to 10 carbon atoms in an aromatic carbocyclic ring. The aryl group may itself be substituted or unsubstituted and, if it is substituted, the substituents are selected from substituents β , defined and exemplified above. Preferably the aralkyl group has a total of from 7 to 11 carbon atoms. The alkyl part

of the aralkyl group may be a straight or branched chain alkyl group having from 1 to 5 carbon atoms. Examples of the unsubstituted aralkyl groups include the benzyl, 2-phenylethyl, 1-phenylethyl, 3-phenylpropyl, 2-phenylpropyl, 1-phenylpropyl, 4-phenylbutyl, 1-phenylbutyl, 5-phenylpentyl, 1-naphthylmethyl and 2-naphthylmethyl groups. Where the aryl part of the aralkyl group is substituted, there is no restriction on the number of substituents, except such as may be imposed by the number of substitutable positions and possibly by steric constraints; thus the maximum number of substituents on a phenyl group is 5, whilst that on a naphthyl group is 7. In general, however, from 1 to 3 substituents are preferred, one substituent generally being more preferred.

Moreover, where substituent β represents an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom or a group of formula $-N(R^a)R^b$, these may be as defined and exemplified above in relation to the corresponding group or atom represented by substituent α . Alternatively, substituent β may be a hydroxy group, a nitro group, a phenyl group or a trifluoromethyl group.

Examples of substituted aralkyl groups which may be represented by substituent α include:

(1) Aralkyl groups substituted by at least one straight or branched chain alkyl group having from 1 to 4 carbon atoms, for example, the 4-methylbenzyl, 4-ethylbenzyl, 4-propylbenzyl, 4-isopropylbenzyl, 4-butylbenzyl, 4-sec-butylbenzyl, 4-tert-butylbenzyl, 4-methyl-1-naphthylmethyl, 5-ethyl-1-naphthylmethyl, 8-propyl-1-naphthylmethyl, 4-isopropyl-1-naphthylmethyl, 5-butyl-1-naphthylmethyl, 4-isobutyl-1-naphthylmethyl, 4-sec-butyl-1-naphthylmethyl, 4-tert-butyl-1-naphthylmethyl, 4-methyl-2-naphthylmethyl, 5-ethyl-2-naphthylmethyl, 8-propyl-2-naphthylmethyl, 4-isopropyl-2-naphthylmethyl, 5-butyl-2-naphthylmethyl, 8-isobutyl-2-naphthylmethyl, 4-sec-butyl-2-naphthylmethyl and 5-tert-butyl-2-naphthylmethyl groups.

(2) Aralkyl groups substituted by at least one straight or branched chain alkoxy group having from 1 to 4 carbon atoms, for example, the 4-methoxybenzyl, 4-ethoxybenzyl, 4-propoxybenzyl, 4-isopropoxybenzyl, 4-butoxybenzyl, 4-sec-butoxybenzyl, 4-tert-butoxybenzyl, 4-methoxy-1-naphthylmethyl, 5-ethoxy-1-naphthylmethyl, 8-propoxy-1-naphthylmethyl, 4-isopropoxy-1-naphthylmethyl, 5-butoxy-1-naphthylmethyl, 4-isobutoxy-1-naphthylmethyl, 4-sec-butoxy-1-naphthylmethyl, 4-tert-butoxy-1-naphthylmethyl, 4-methoxy-2-naphthylmethyl, 5-ethoxy-2-naphthylmethyl, 8-propoxy-2-naphthylmethyl, 4-isopropoxy-2-naphthylmethyl, 5-butoxy-2-naphthylmethyl, 8-isobutoxy-2-naphthylmethyl, 4-sec-butoxy-2-naphthylmethyl and 5-tert-butoxy-2-naphthylmethyl groups.

(3) Aralkyl groups substituted by at least one halogen atom, for example, the 4-bromobenzyl, 4-chlorobenzyl, 4-fluorobenzyl, 4-iodobenzyl, 3-chlorobenzyl, 3-fluorobenzyl, 3-bromobenzyl, 3-iodobenzyl, 4-bromo-1-naphthylmethyl, 4-chloro-1-naphthylmethyl, 4-fluoro-1-naphthylmethyl, 4-iodo-1-naphthylmethyl, 5-chloro-1-naphthylmethyl, 5-fluoro-1-naphthylmethyl, 5-bromo-1-naphthylmethyl, 8-chloro-1-naphthylmethyl, 4-fluoro-2-naphthylmethyl, 4-bromo-2-naphthylmethyl, 4-chloro-2-naphthylmethyl, 4-iodo-2-naphthylmethyl, 5-bromo-2-naphthylmethyl, 5-chloro-2-naphthylmethyl, 5-fluoro-2-naphthylmethyl and 5-iodo-2-naphthylmethyl groups.

(4) Aralkyl groups substituted by at least one hydroxy group, for example, the 2-hydroxybenzyl, 3-hydroxybenzyl, 4-hydroxybenzyl, 4-hydroxy-1-naphthylmethyl, 5-hydroxy-1-naphthylmethyl, 8-hydroxy-1-naphthylmethyl, 4-hydroxy-2-naphthylmethyl, 5-hydroxy-2-naphthylmethyl and 8-hydroxy-2-naphthylmethyl groups.

(5) Aralkyl groups substituted by at least one nitro group, for example, the 2-nitrobenzyl, 3-nitrobenzyl, 4-nitrobenzyl, 4-nitro-1-naphthylmethyl, 5-nitro-1-naphthylmethyl, 8-nitro-1-naphthylmethyl, 4-nitro-2-naphthylmethyl, 5-nitro-2-naphthylmethyl and 8-nitro-2-naphthylmethyl groups.

(6) Aralkyl groups substituted by at least one phenyl group, for example, the 3-phenylbenzyl, 4-phenylbenzyl, 4-phenyl-1-naphthylmethyl, 5-phenyl-1-naphthylmethyl, 8-phenyl-1-naphthylmethyl, 4-phenyl-2-naphthylmethyl, 5-phenyl-2-naphthylmethyl and 8-phenyl-2-naphthylmethyl groups.

(7) Aralkyl groups substituted by at least one trifluoromethyl group, for example, the 3-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-trifluoromethyl-1-naphthylmethyl, 5-trifluoromethyl-1-naphthylmethyl, 8-trifluoromethyl-1-naphthylmethyl, 4-trifluoromethyl-2-naphthylmethyl, 5-trifluoromethyl-2-naphthylmethyl and 8-trifluoromethyl-2-naphthylmethyl groups.

(8) Aralkyl groups substituted by at least one unsubstituted amino group, i.e. by a group of formula $-N(R^a)R^b$, where R^a and R^b both represent hydrogen atoms, for example, the 2-aminobenzyl, 3-aminobenzyl, 4-aminobenzyl, 4-amino-1-naphthylmethyl and 8-amino-2-naphthylmethyl groups.

(9) Aralkyl groups substituted by at least one substituted amino group, examples of which include:

(i) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an alkyl group, for example, the 3-methylaminobenzyl, 4-ethylaminobenzyl, 3-propylaminobenzyl, 3-isopropylaminobenzyl, 4-butylaminobenzyl and 3-isobutylaminobenzyl groups;

(ii) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aralkyl group, for example, the 4-benzylaminobenzyl, 4-(2-phenylethylamino)benzyl, 4-(1-phenylethylamino)benzyl, 4-(4-phenylbutylamino)benzyl and 4-(1-naphthylmethylamino)benzyl groups;

(iii) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aryl group, for example, the 4-phenylaminobenzyl and 4-(1-naphthylamino)benzyl groups;

(iv) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aliphatic acyl group, for example, the 4-formylaminobenzyl, 4-acetylaminobenzyl, 4-butyrylaminobenzyl, 4-pivaloylaminobenzyl, 4-hexanoylaminobenzyl, 4-octanoylaminobenzyl and 4-undecanoylaminobenzyl groups;

(v) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aryl-aliphatic acyl group, for example, the 4-phenylacetylaminobenzyl, 4-(4-phenylbutylamino)benzyl, 4-(6-phenylhexanoylaminobenzyl, 4-(α -methylphenylacetylaminobenzyl and 4-(α,α -dimethylphenylacetylaminobenzyl groups;

(vi) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents a hydrogen atom and R^b represents an aromatic acyl group, for example, the 4-benzoylaminobenzyl, 4-(1-naphthoylaminobenzyl and 4-(2-naphthoylaminobenzyl groups;

(vii) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a and R^b both represent alkyl groups which may be the same or different, for example, the 4-dimethylaminobenzyl, 4-diethylaminobenzyl and 4-(N -methyl- N -ethylamino)benzyl groups;

(viii) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aralkyl group, for example, the 4-(N -ethyl- N -benzylamino)benzyl, 4-(N -t-butyl- N -benzylamino)benzyl and 4-(N -ethyl- N -benzylamino)benzyl groups;

(ix) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aryl group, for example, the 4-(N -methyl- N -phenylamino)benzyl and 4-(N -octyl- N -phenylamino)benzyl groups;

(x) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aliphatic acyl group, for example, the 4-(N -propyl- N -acetylaminobenzyl and 4-(N -ethyl- N -hexanoylaminobenzyl groups;

(xi) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N -ethyl- N -phenylacetylaminobenzyl and 4-(N -methyl- N -(6-phenylhexanoylaminobenzyl groups;

(xii) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an alkyl group and R^b represents an aromatic acyl group, for example, the 4-(N -methyl- N -benzoylaminobenzyl and 4-(N -heptyl- N -benzoylaminobenzyl groups;

(xiii) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a and R^b both represent aralkyl groups which may be the same or different, for example, the 4-dibenzylaminobenzyl and 4-(N -benzyl- N -(2-naphthylmethylamino)benzyl groups;

(xiv) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an aralkyl group and R^b represents an aryl group, for example, the 4-(N -benzyl- N -phenylamino)benzyl and 4-(N -(3-phenylpropyl)- N -phenylamino)benzyl groups;

(xv) aralkyl groups substituted by a group of formula $-NR^aR^b$, where R^a represents an aralkyl group and R^b

represents an aliphatic acyl group, for example, the 4-(N-benzyl-N-acetyl amino)benzyl and 4-(N-benzyl-N-pentanoyl amino)benzyl groups;

(xvi) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aralkyl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N-benzyl-N-phenylacetyl amino)benzyl and 4-(N-benzyl-N-(4-phenylbutyl) amino)benzyl groups;

(xvii) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aralkyl group and R^b represents an aromatic acyl group, for example, the 4-(N-benzyl-N-benzoyl amino)benzyl and 4-(N-(2-phenylethyl)-N-benzoyl amino)benzyl groups;

(xviii) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aryl groups which may be the same or different, for example, the 4-diphenyl amino benzyl and 4-(N-(2-naphthyl)-N-phenyl amino)benzyl groups;

(xix) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl group and R^b represents an aliphatic acyl group, for example, the 4-(N-phenyl-N-acetyl amino)benzyl and 4-(N-phenyl-N-hexanoyl amino)benzyl groups;

(xx) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N-phenyl-N-phenylacetyl amino)benzyl and 4-(N-phenyl-N-(4-phenylbutyl) amino)benzyl groups;

(xxi) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl group and R^b represents an aromatic acyl group, for example, the 4-(N-phenyl-N-benzoyl amino)benzyl group;

(xxii) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aliphatic acyl groups which may be the same or different, for example, the 4-diacyl amino benzyl and 4-(N-butyl-N-hexanoyl amino)benzyl groups;

(xxiii) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aliphatic acyl group and R^b represents an aryl-aliphatic acyl group, for example, the 4-(N-acetyl-N-phenylacetyl amino)benzyl and 4-(N-butyl-N-(2-phenylethyl) amino)benzyl groups;

(xxiv) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aliphatic acyl group and R^b represents an aromatic acyl group, for example, the 4-(N-acetyl-N-benzoyl amino)benzyl and 4-(N-butyl-N-(2-naphthyl) amino)benzyl groups;

(xxv) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aryl-aliphatic acyl groups which may be the same or different, for example, the 4-(N-N-diphenylacetyl amino)benzyl and 4-(N-phenylacetyl-N-(4-phenylbutyl) amino)benzyl groups;

(xxvi) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a represents an aryl-aliphatic acyl group and R^b represents an aromatic acyl group, for example, the 4-(N-phenylacetyl-N-benzoyl amino)benzyl and 4-(N-phenylacetyl-N-(2-naphthyl) amino)benzyl groups; and

(xxvii) aralkyl groups substituted by a group of formula -NR^aR^b, where R^a and R^b both represent aromatic acyl groups which may be the same or different, for example, the 4-dibenzoyl amino benzyl and 4-(N-benzoyl-N-(2-naphthyl) amino)benzyl groups.

Where the benzimidazole group represented by X has a substituent α at the 1- and/or 2-position, the substituent α is preferably:

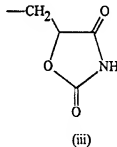
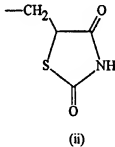
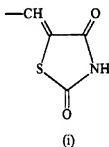
a straight or branched chain alkyl group having from 1 to 4 carbon atoms,

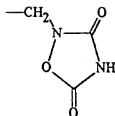
an aryl group having from 6 to 10 carbon atoms which may optionally be substituted by one or more substituents β , or

a straight or branched chain alkyl group having from 7 to 11 carbon atoms which may optionally be substituted by one or more substituents β .

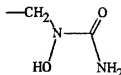
Examples of such benzimidazole groups having from 1 to 5 of substituents α include, for example, the 1-methylbenzimidazol-2-yl, 1-ethylbenzimidazol-2-yl, 1-propylbenzimidazol-2-yl, 1-isopropylbenzimidazol-2-yl, 1-butylbenzimidazol-2-yl, 6-methoxy-1H-benzimidazol-2-yl, 5-methoxy-1H-benzimidazol-2-yl, 6-methoxy-1-methylbenzimidazol-2-yl, 5-methoxy-1-methylbenzimidazol-2-yl, 1-ethyl-6-methoxybenzimidazol-2-yl, 1-ethyl-5-methoxybenzimidazol-2-yl, 6-methoxy-1-propylbenzimidazol-2-yl, 5-methoxy-1-propylbenzimidazol-2-yl, 1-isopropyl-6-methoxybenzimidazol-2-yl, 1-isopropyl-5-methoxybenzimidazol-2-yl, 1-isobutyl-6-methoxybenzimidazol-2-yl, 1-isobutyl-5-methoxybenzimidazol-2-yl, 1-methyl-5-propoxybenzimidazol-2-yl, 5-ethoxy-1-methylbenzimidazol-2-yl, 1-methyl-6-propoxybenzimidazol-2-yl, 1-methyl-5-propoxybenzimidazol-2-yl, 6-isopropoxy-1-methylbenzimidazol-2-yl, 5-isopropoxy-1-methylbenzimidazol-2-yl, 6-butoxy-1-methylbenzimidazol-2-yl, 5-butoxy-1-methylbenzimidazol-2-yl, 6-isobutoxy-1-methylbenzimidazol-2-yl, 5-isobutoxy-1-methylbenzimidazol-2-yl, 6-sec-butoxy-1-methylbenzimidazol-2-yl, 5-sec-butoxy-1-methylbenzimidazol-2-yl, 6-tert-butoxy-1-methylbenzimidazol-2-yl, 5-tert-butoxy-1-methylbenzimidazol-2-yl, 6-butoxy-1-propylbenzimidazol-2-yl, 6-benzyloxy-1-methylbenzimidazol-2-yl, 5-benzyloxy-1-methylbenzimidazol-2-yl, 5-methoxy-1,6-dimethylbenzimidazol-2-yl, 6-methoxy-1,5-dimethylbenzimidazol-2-yl, 6-bromo-5-methoxy-1-methylbenzimidazol-2-yl, 5-bromo-6-methoxy-1-methylbenzimidazol-2-yl, 5-ethoxy-6-fluoro-1-methylbenzimidazol-2-yl, 6-ethoxy-5-fluoro-1-methylbenzimidazol-2-yl, 5,7-difluoro-1-methylbenzimidazol-2-yl, 4,6-difluoro-1-methylbenzimidazol-2-yl, 6-fluoro-1-methylbenzimidazol-2-yl, 5-fluoro-1-methylbenzimidazol-2-yl, 5-chloro-1,6-dimethylbenzimidazol-2-yl, 6-chloro-1,5-dimethylbenzimidazol-2-yl, 5-chloro-1,6-diethylbenzimidazol-2-yl, 6-chloro-1,5-diethylbenzimidazol-2-yl, 5-ethyl-1-methylbenzimidazol-2-yl, 6-ethyl-1-methylbenzimidazol-2-yl, 5-bromo-1-methylbenzimidazol-2-yl, 6-bromo-1-methylbenzimidazol-2-yl, 7-bromo-1-methyl-5-trifluoromethylbenzimidazol-2-yl, 4-bromo-1-methyl-6-trifluoromethylbenzimidazol-2-yl, 7-chloro-1-methyl-5-trifluoromethylbenzimidazol-2-yl, 4-chloro-1-methyl-6-trifluoromethylbenzimidazol-2-yl, 1-methyl-7-trifluoromethylbenzimidazol-2-yl, 1-methyl-4-trifluoromethylbenzimidazol-2-yl, 1-methyl-5-trifluoromethylbenzimidazol-2-yl, 1-methyl-6-trifluoromethylbenzimidazol-2-yl, 5-bromo-1,6,7-trimethylbenzimidazol-2-yl, 6-bromo-1,4,5-trimethylbenzimidazol-2-yl, 5-fluoro-6-chloro-1-methylbenzimidazol-2-yl, 6-fluoro-5-chloro-1-methylbenzimidazol-2-yl, 5-bromo-1,7-dimethylbenzimidazol-2-yl, 6-bromo-1,4-dimethylbenzimidazol-2-yl, 6-tert-butyl-1-methylbenzimidazol-2-yl, 5-tert-butyl-1-methylbenzimidazol-2-yl, 6-hydroxy-1-methylbenzimidazol-2-yl, 5-hydroxy-1-methylbenzimidazol-2-yl, 1,7-dimethylbenzimidazol-2-yl, 1,4-dimethylbenzimidazol-2-yl, 6,7-dichloro-1-methylbenzimidazol-2-yl, 4,5-dichloro-1-methylbenzimidazol-2-yl, 5,6,7-trifluoro-1-methylbenzimidazol-2-yl, 4,5,6-trifluoro-1-methylbenzimidazol-2-yl, 5-bromo-6-benzyloxy-1-methylbenzimidazol-2-yl, 7-chloro-1-methylbenzimidazol-2-yl, 4-chloro-1-methylbenzimidazol-2-yl, 6-hydroxy-1,5,7-trimethylbenzimidazol-2-yl, 5-hydroxy-1,4,6-trimethylbenzimidazol-2-yl, 1-methylbenzimidazol-6-yl, 1-ethylbenzimidazol-6-yl, 1-propylbenzimidazol-6-yl, 1-isopropylbenzimidazol-6-yl, 1-butylbenzimidazol-6-yl, 1-benzylbenzimidazol-6-yl, 1-methylbenzimidazol-7-yl, 1-ethylbenzimidazol-7-yl, 1-benzylbenzimidazol-7-yl, 1-methylbenzimidazol-4-yl, 1-methylbenzimidazol-5-yl, 1,2-dimethylbenzimidazol-6-yl, 5-hydroxy-1,4,6,7-tetramethylbenzimidazol-2-yl, 1-ethyl-5-hydroxy-4,6,7-trimethylbenzimidazol-2-yl, 1-benzylbenzimidazol-5-yl and 5-acetoxy-1,4,6,7-tetramethylbenzimidazol-2-yl groups.

Z represents a group of formula (i), (ii), (iii), (iv) or (v):





(iv)



(v)

These formulae (i), (ii), (iii), (iv) and (v) are hereinafter referred to as the 2,4-dioxothiazolidin-5-ylidenylmethyl group, the 2,4-dioxothiazolidin-5-ylmethyl group, the 2,4-dioxoxazolidin-5-ylmethyl group, the 3,5-dioxoxazolidin-2-ylmethyl group and the N-hydroxyureidomethyl group, respectively. Of these, the 2,4-dioxothiazolidin-5-ylidenylmethyl, 2,4-dioxothiazolidin-5-ylmethyl and 2,4-dioxoxazolidin-5-ylmethyl groups are preferred, the 2,4-dioxothiazolidin-5-ylidenylmethyl and 2,4-dioxothiazolidin-5-ylmethyl groups being more preferred and the 2,4-dioxothiazolidin-5-ylmethyl group being most preferred.

Of the compounds of the present invention, we prefer those compounds of formula (I) and salts thereof, in which:

(A1) X represents a benzimidazole group, which is unsubstituted or is substituted by from 1 to 5 of substituents α' , defined below;

substituent α' represents an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms, a benzyloxy group, a halogen atom, a hydroxy group, an acetoxy group, a phenylthio group, an alkylthio group having from 1 to 4 carbon atoms, a trifluoromethyl group, a nitro group, an amino group of formula $-NR^aR^b$,

in which R^a and R^b are the same or different and each represents a hydrogen atom, an alkyl group having from 1 to 8 carbon atoms, an aralkyl group having from 7 to 11 carbon atoms, an aryl group having from 6 to 10 carbon atoms, an aliphatic acyl group having from 1 to 11 carbon atoms, an aryl-aliphatic acyl group having from 6 to 12 carbon atoms or an aromatic acyl group having from 7 to 11 carbon atoms,

an aryl group having from 6 to 10 carbon atoms which is unsubstituted or is substituted by at least one of substituents β ,

said substituent β represents an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom, a hydroxy group, a nitro group, a phenyl group, a trifluoromethyl group or an amino group of formula $-NR^aR^b$, in which R^a and R^b are as defined above;

or an aralkyl group having from 7 to 11 carbon atoms which is unsubstituted or is substituted by at least one of substituents β ;
and/or

(A2) R represents a hydrogen atom, an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms or a halogen atom;

and especially compounds in which X is as defined in (A1) and R is as defined in (A2).

More preferred compounds of the present invention are those compounds of formula (I) and salts thereof, in which:

(B1) X represents a benzimidazole group, which is unsubstituted or is substituted by from 1 to 5 of substituents α' , defined in (A1) above,
and/or

(B2) Y represents an oxygen atom;
and/or

(B3) Z represents a 2,4-dioxothiazolidin-5-ylidenylmethyl, 2,4-dioxothiazolidin-5-ylmethyl or 2,4-dioxoxazolidin-5-ylmethyl group;

and/or

(B4) R represents a hydrogen atom, an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms or a halogen atom;

and especially compounds in which X is as defined in (B1), Y is as defined in (B2), Z is as defined in (B3), and R is as defined in (B4).

Still more preferred compounds of the present invention are those compounds of formula (I) and salts thereof, in which:

(C1) X represents a benzimidazole group, which is unsubstituted or is substituted by from 1 to 5 of substituents α' , defined in (A1) above;
and/or

(C2) Y represents an oxygen atom;
and/or

(C3) Z represents a 2,4-dioxothiazolidin-5-ylidenylmethyl or 2,4-dioxothiazolidin-5-ylmethyl group;
and/or

(C4) R represents a hydrogen atom, a methyl group, a methoxy group, an ethoxy group, a fluorine atom or a chlorine atom;
and/or

(C5) \underline{m} represents an integer from 1 to 3;

and especially compounds in which X is as defined in (C1), Y is as defined in (C2), Z is as defined in (C3), R is as defined in (C4), and \underline{m} is as defined in (C5).

Still more preferred compounds of the present invention are those compounds of formula (I) and salts thereof, in which:

(D1) X represents a benzimidazole group, which is unsubstituted or is substituted by from 1 to 5 of substituents α'' , defined below;

substituent α'' represents an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms, a benzyloxy group, a halogen atom, a phenylthio group, an alkylthio group having from 1 to 4 carbon atoms, a trifluoromethyl group, a hydroxy group, an acetoxy group, a benzyl group or a phenyl group;
and/or

(D2) Y represents an oxygen atom;
and/or

(D3) Z represents a 2,4-dioxothiazolidin-5-ylmethyl group;
and/or

(D4) R represents a hydrogen atom, a methyl group or a methoxy group;
and/or

(D5) \underline{m} represents an integer from 1 to 3;

and especially compounds in which X is as defined in (D1), Y is as defined in (D2), Z is as defined in (D3), R is as defined in (D4), and \underline{m} is as defined in (D5).

Yet more preferred compounds of the present invention are those compounds of formula (I) and salts thereof, in which:

(E1) X represents a benzimidazole group, which is unsubstituted or is substituted by from 1 to 5 of substituents α''' , defined below;

substituent α''' represents a methyl group, an ethyl group, an isopropyl group, a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a benzyloxy group, a fluorine atom, a chlorine atom, a phenylthio

group, a methylthio group, an ethylthio group, a hydroxy group, an acetoxy group, a benzyl group or a phenyl group;
and/or

(E2) Y represents an oxygen atom;
and/or

(E3) Z represents a 2,4-dioxothiazolidin-5-ylmethyl group;
and/or

(E4) R represents a hydrogen atom;
and/or

(E5) \underline{m} represents the integer 1 or 2;

and especially compounds in which X is as defined in (E1), Y is as defined in (E2), Z is as defined in (E3), R is as defined in (E4), and \underline{m} is as defined in (E5).

The most preferred compounds of the present invention are those compounds of formula (I) and salts thereof, in which:

(F1) X represents a benzimidazole group, which is unsubstituted or is substituted by from 1 to 5 of substituents α^* , defined below;
substituent α^* represents a methyl group, a methoxy group, a hydroxy group, a benzyl group or an acetoxy group;
and/or

(F2) Y represents an oxygen atom;
and/or

(F3) Z represents a 2,4-dioxothiazolidin-5-ylmethyl group;
and/or

(F4) R represents a hydrogen atom;
and/or

(F5) \underline{m} represents the integer 1;

and especially compounds in which X is as defined in (F1), Y is as defined in (F2), Z is as defined in (F3), R is as defined in (F4), and \underline{m} is as defined in (F5).

The compounds of the present invention each contains a basic group in its molecule, and each can thus be converted to a salt with an acid by conventional methods. There is no particular restriction on the nature of such salts, provided that, where the resulting salts are to be used medically, these salts are pharmaceutically acceptable, that is they are not less active, or unacceptably less active, nor more toxic, or unacceptably more toxic, than the parent compound. However, where the resulting salt is to be used for non-medical uses, e.g. as an intermediate in the preparation of other compounds, even this restriction does not apply, and there is then no restriction on the nature of the salts which may be formed. Examples of such salts include: salts with mineral acids, especially hydrohalic acids (such as hydrofluoric acid, hydrobromic acid, hydroiodic acid or hydrochloric acid), nitric acid, perchloric acid, carbonic acid, sulphuric acid or phosphoric acid; salts with lower alkylsulphonic acids, such as methanesulphonic acid, trifluoromethanesulphonic acid or ethanesulphonic acid; salts with arylsulphonic acids, such as benzenesulphonic acid or *p*-toluenesulphonic acid; salts with organic carboxylic acids, such as acetic acid, fumaric acid, tartaric acid, oxalic acid, maleic acid, malic acid, succinic acid, benzoic acid, mandelic acid, ascorbic acid, lactic acid, gluconic acid or citric acid; and salts with amino acids, such as glutamic acid or aspartic acid. We prefer the pharmaceutically acceptable salts.

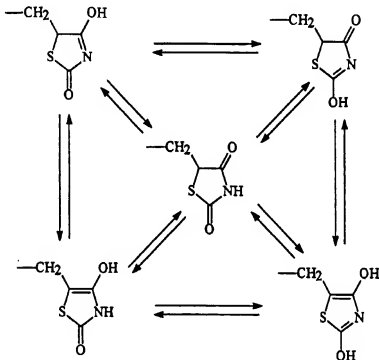
Also, the compound of the present invention can be converted into a salt with a base by conventional methods. Examples of such salts include: salts with an alkali metal, such as sodium, potassium or lithium; salts with an alkaline earth metal, such as barium or calcium; and salts with another metal, such as magnesium or aluminium. We prefer the pharmaceutically acceptable salts.

The compounds of formula (I) of the present invention can exist in the form of various isomers due to the presence of asymmetric carbon atoms. Thus, where Z represents a 2,4-dioxothiazolidin-5-ylmethyl or 2,4-dioxoxazolidin-5-ylmethyl group, the carbon atom at the 5-position is asymmetric. Although these isomers are all represented herein by

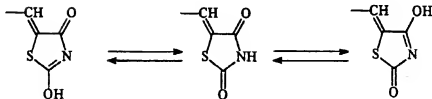
a single molecular formula (I), the present invention includes both the individual, isolated isomers and mixtures, including racemates, thereof and the isomers may be present in such mixtures in any proportions. Where stereospecific synthesis techniques are employed or optically active compounds are employed as starting materials, individual isomers may be prepared directly; on the other hand, if a mixture of isomers is prepared, the individual isomers may be obtained by conventional resolution techniques. Alternatively, a mixture of isomers may be employed.

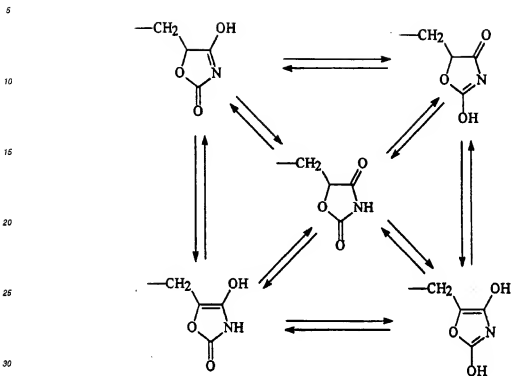
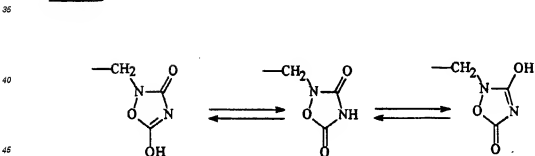
The compounds of formula (I) in which Z represents a 2,4-dioxothiazolidin-5-ylmethyl, 2,4-dioxothiazolidin-5-ylidenemethyl, 2,4-dioxoxazolidin-5-ylmethyl or 3,5-dioxoxazolidin-2-ylmethyl group can exist in the form of various tautomeric isomers as shown in the following schemes α , β , γ and δ , respectively:

Scheme α



Scheme β



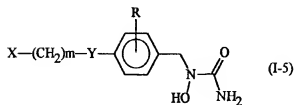
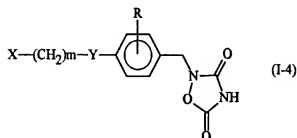
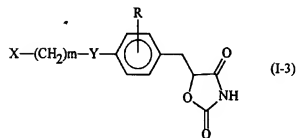
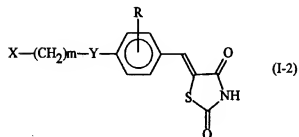
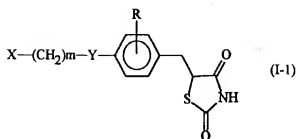
Scheme 7Scheme 8

In the above formula (I), all tautomers based thereon and mixtures of equivalent weights or non-equivalent weights of these tautomers are represented by one formula. Thus, all of these isomers and mixtures of these isomers are included in the present invention.

Moreover, the present invention also includes all solvates, for example hydrates, of the compounds of formula (I) and salts thereof, where the relevant compound is capable of forming a solvate.

The invention also embraces all compounds which could be converted in the living mammalian, for example human, body to a compound of formula (I) or a salt thereof by the action of the metabolism, that is so-called "pro-drugs" of the compounds of formula (I) and salts thereof.

Examples of certain compounds of the present invention are given in the following formulae (I-1) to (I-5):



In the above formulae, the substituents are as defined in the following one of Tables 1 to 5, respectively. That is, Table 1 relates to formula (I-1), Table 2 relates to formula (I-2), and so on to Table 5, which relates to formula (I-5). In

the Tables, the following abbreviations are used:

Bu	butyl
iBu	isobutyl
sBu	sec-butyl
tBu	t-butyl
Bz	benzyl
Et	ethyl
Me	methyl
Pr	propyl
iPr	isopropyl

Table 1









Compound No.	X	Y	m	R
1-1		0	1	H
1-2		0	2	H
1-3		0	3	H
1-4		0	4	H
1-5		0	5	MeO
1-6		S	1	H
1-7		O	1	MeO
1-8		O	1	Cl

Table 1 (cont.)









Compound No.	X	Y	m	R
1-9		O	1	Me
1-10		S	1	MeO
1-11		O	1	H
1-12		O	2	H
1-13		O	3	H
1-14		O	- 4	H
1-15		O	5	H
1-16		S	1	H

Table 1 (cont.)









Compound No.	X	Y	m	R
1-17		S	2	H
1-18		O	1	MeO
1-19		O	1	EtO
1-20		O	1	Cl
1-21		O	1	F
1-22		O	1	Me
1-23		O	1	<i>i</i> Pr
1-24		O	2	Et

Table 1 (cont.)









Compound No.	X	Y	m	R
1-25		S	1	Cl
1-26		S	1	Me
1-27		O	1	H
1-28		O	2	H
1-29		O	3	<i>t</i> Bu
1-30		O	1	Me
1-31		O	1	MeO
1-32		S	1	H

Table 1 (cont.)








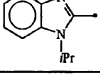
Compound No.	X	Y	m	R
1-33		S	1	PrO
1-34		S	1	Me
1-35		O	1	H
1-36		O	3	H
1-37		O	1	F
1-38		S	1	H
1-39		O	1	H
1-40		O	2	H

Table 1 (cont.)

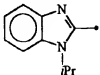
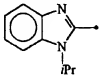
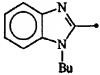
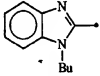
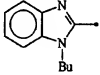
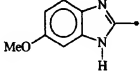
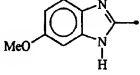
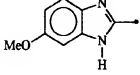
Compound No.	X	Y	m	R
1-41		S	1	H
1-42		S	5	Cl
1-43		O	1	H
1-44		O	4	H
1-45		S	1	H
1-46		O	1	H
1-47		O	3	H
1-48		S	1	H

Table 1 (cont.)

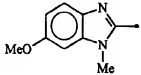
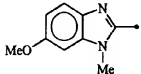
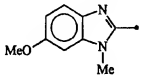
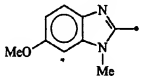
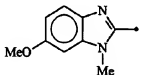
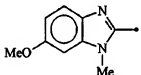
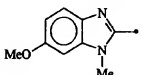
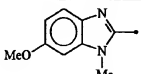
Compound No.	X	Y	m	R
1-49		O	1	H
1-50		O	2	H
1-51		O	3	H
1-52		O	4	H
1-53		O	5	H
1-54		S	1	H
1-55		S	2	H
1-56		O	1	Me

Table 1 (cont.)

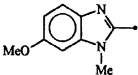
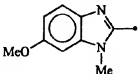
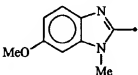
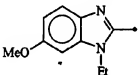
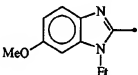
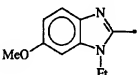
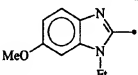
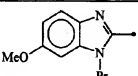
Compound No.	X	Y	m	R
1-57		O	1	MeO
1-58		O	1	F
1-59		O	1	Cl
1-60		O	1	H
1-61		O	2	H
1-62		O	1	MeO
1-63		S	1	H
1-64		O	1	H

Table 1 (cont.)

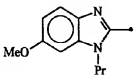
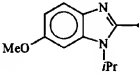
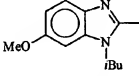
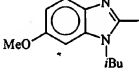
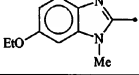
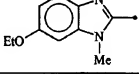
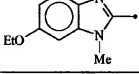
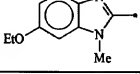
Compound No.	X	Y	m	R
1-65		S	1	H
1-66		O	1	H
1-67		O	1	H
1-68		S	1	H
1-69		O	1	H
1-70		O	1	MeO
1-71		O	1	Cl
1-72		O	2	H

Table 1 (cont.)

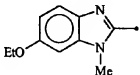
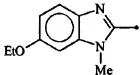
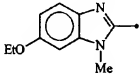
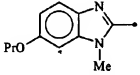
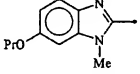
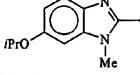
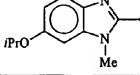
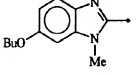
Compound No.	X	Y	m	R
1-73		O	3	H
1-74		S	1	H
1-75		S	4	Et
1-76		O	1	H
1-77		S	1	H
1-78		O	1	H
1-79		O	3	H
1-80		O	1	H

Table 1 (cont.)

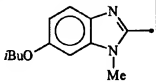
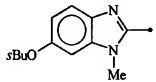
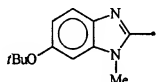
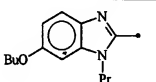
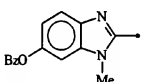
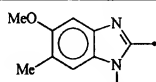
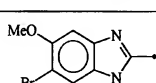
Compound No.	X	Y	m	R
1-81		O	1	H
1-82		O	1	H
1-83		O	1	H
1-84		O	1	H
1-85		O	1	H
1-86		O	1	H
1-87		O	1	H

Table 1 (cont.)

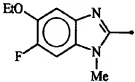
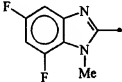
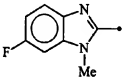
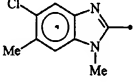
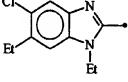
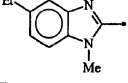
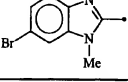
Compound No.	X	Y	m	R
1-88		O	1	H
1-89		O	1	H
1-90		O	1	H
1-91		O	1	H
1-92		O	1	H
1-93		O	1	H
1-94		O	1	H

Table 1 (cont.)

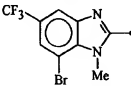
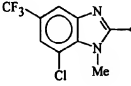

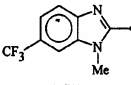
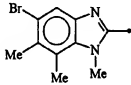
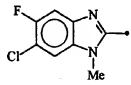
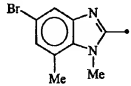
Compound No.	X	Y	m	R
1-95		O	1	H
1-96		O	1	H
1-97		O	1	H
1-98		O	1	H
1-99		O	1	H
1-100		O	1	H
1-101		O	1	H

Table 1 (cont.)

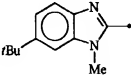
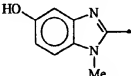

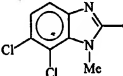
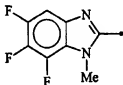
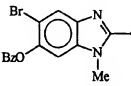

Compound No.	X	Y	m	R
1-102		O	1	H
1-103		O	1	H
1-104		O	1	H
1-105		O	1	H
1-106		O	1	H
1-107		O	1	H
1-108		O	1	H

Table 1 (cont.)








Compound No.	X	Y	m	R
1-116		O	1	H
1-117		S	1	H
1-118		O	1	H
1-119		O	2	H
1-120		O	3	H
1-121		O	4	H
1-122		O	5	H

Table 1 (cont.)








Compound No.	X	Y	m	R
1-123		O	1	MeO
1-124		O	1	Cl
1-125		S	1	H
1-126		S	3	H
1-127		O	1	H
1-128		S	1	H
1-129		O	1	H

Table 1 (cont.)

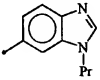
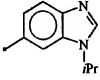
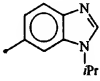
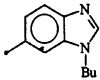
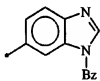
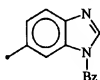
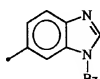
Compound No.	X	Y	m	R
1-130		O	1	Cl
1-131		O	1	H
1-132		S	1	H
1-133		O	1	H
1-134		O	1	H
1-135		O	3	H
1-136		S	1	H

Table 1 (cont.)








Compound No.	X	Y	m	R
1-137		O	1	H
1-138		O	1	H
1-139		O	1	H
1-140		S	1	H
1-141		O	1	H
1-142		O	1	H
1-143		O	1	H

Table 1 (cont.)

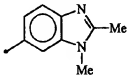
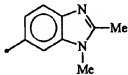
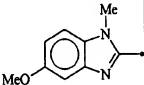
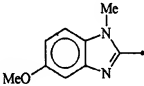
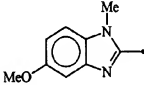
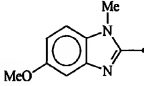
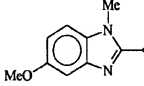
Compound No.	X	Y	m	R
1-144		O	1	H
1-145		S	1	H
1-146		O	1	H
1-147		O	2	H
1-148		O	3	H
1-149		O	4	H
1-150		O	5	H

Table 1 (cont.)

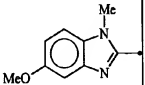
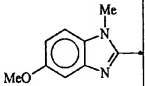
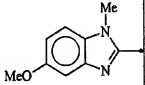
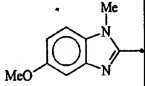
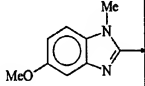
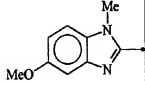
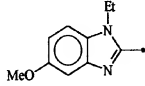
Compound No.	X	Y	m	R
1-151		S	1	H
1-152		S	2	H
1-153		O	1	Me
1-154		O	2	Me
1-155		O	1	F
1-156		O	1	Cl
1-157		O	1	H

Table 1 (cont.)

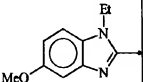
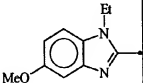
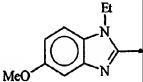
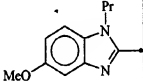
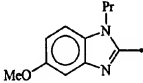
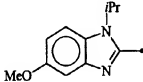
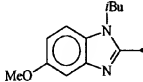
Compound No.	X	Y	m	R
1-158		O	2	H
1-159		O	1	MeO
1-160		S	1	H
1-161		O	1	H
1-162		S	1	H
1-163		O	1	H
1-164		O	1	H

Table 1 (cont.)

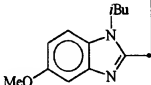
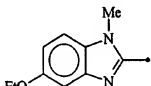
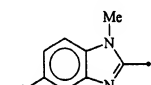
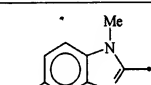
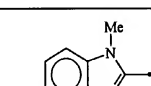
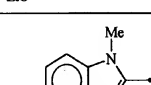
Compound No.	X	Y	m	R
1-165		S	1	H
1-166		O	1	H
1-167		O	1	MeO
1-168		O	1	Cl
1-169		O	2	H
1-170		O	3	H

Table 1 (cont.)

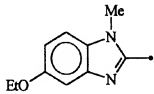
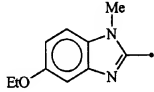
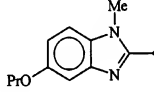
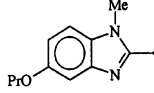
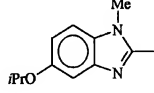
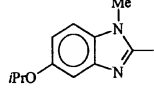
Compound No.	X	Y	m	R
1-171		S	1	H
1-172		S	4	Et
1-173		O	1	H
1-174		S	1	H
1-175		O	1	H
1-176		O	3	H

Table 1 (cont.)

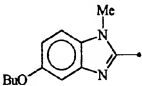
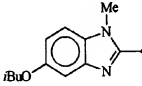
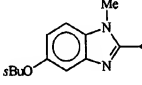
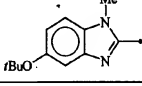
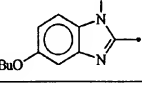
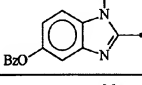
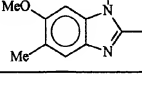
Compound No.	X	Y	m	R
1-177		O	1	H
1-178		O	1	H
1-179		O	1	H
1-180		O	1	H
1-181		O	1	H
1-182		O	1	H
1-183		O	1	H

Table 1 (cont.)

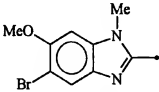
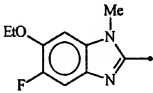
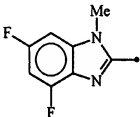
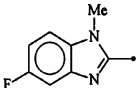
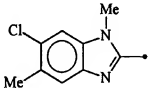
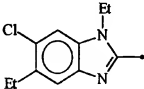
Compound No.	X	Y	m	R
1-184		O	1	H
1-185		O	1	H
1-186		O	1	H
1-187		O	1	H
1-188		O	1	H
1-189		O	1	H

Table 1 (cont.)

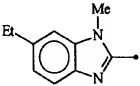
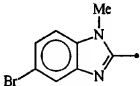
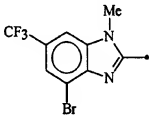
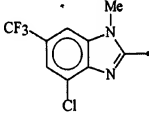
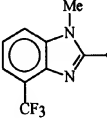
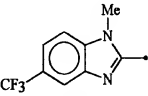
Compound No.	X	Y	m	R
1-190		O	1	H
1-191		O	1	H
1-192		O	1	H
1-193		O	1	H
1-194		O	1	H
1-195		O	1	H

Table 1 (cont.)

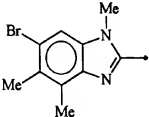
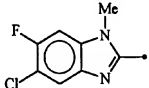
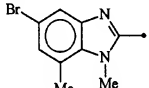
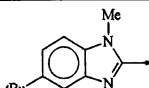
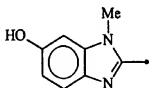
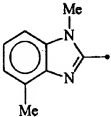
Compound No.	X	Y	m	R
1-196		O	1	H
1-197		O	1	H
1-198		O	2	H
1-199		O	1	H
1-200		O	1	H
1-201		O	1	H

Table 1 (cont.)

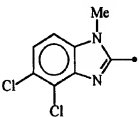
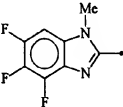
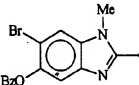
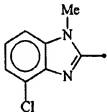
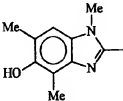
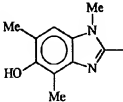
Compound No.	X	Y	m	R
1-202		O	1	H
1-203		O	1	H
1-204		O	1	H
1-205		O	1	H
1-206		O	1	H
1-207		O	2	H

Table 1 (cont.)

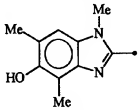
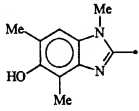
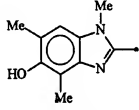
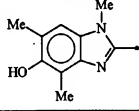
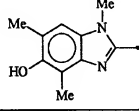

Compound No.	X	Y	m	R
1-208		O	3	H
1-209		S	1	H
1-210		O	1	Me
1-211		O	1	MeO
1-212		O	1	Cl
1-213		O	1	H

Table 1 (cont.)









Compound No.	X	Y	m	R
1-214		O	2	H
1-215		O	3	H
1-216		O	4	H
1-217		O	5	H
1-218		O	1	MeO
1-219		O	1	Cl
1-220		S	1	H
1-221		S	3	H

Table 1 (cont.)









Compound No.	X	Y	m	R
1-222		O	1	H
1-223		S	1	H
1-224		O	1	H
1-225		O	1	Cl
1-226		O	1	H
1-227		S	1	H
1-228		O	1	H
1-229		O	1	H

Table 1 (cont.)



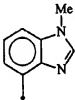
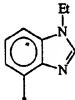
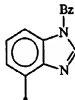

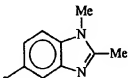
Compound No.	X	Y	m	R
1-230		O	3	H
1-231		S	1	H
1-232		O	1	H
1-233		O	1	H
1-234		O	1	H
1-235		S	1	H
1-236		O	1	H

Table 1 (cont.)

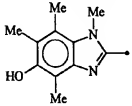
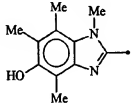
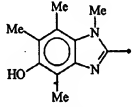
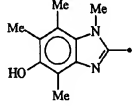
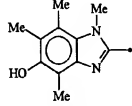
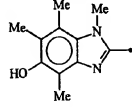
Compound No.	X	Y	m	R
1-237		O	1	H
1-238		O	2	H
1-239		O	3	H
1-240		O	4	H
1-241		S	1	H
1-242		O	1	MeO

Table 1 (cont.)

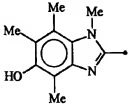
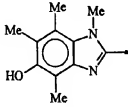
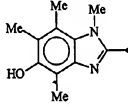
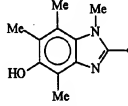
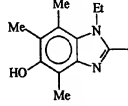
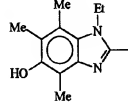
Compound No.	X	Y	m	R
1-243		O	1	Cl
1-244		O	1	F
1-245		O	1	CF ₃
1-246		O	1	Et
1-247		O	1	H
1-248		O	2	H

Table 1 (cont.)

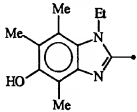
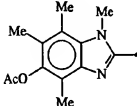
Compound No.	X	Y	m	R
1-249		O	1	MeO
1-250		O	1	H

Table 2








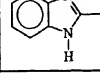
Compound No.	X	Y	m	R
2-1		0	1	H
2-2		0	2	H
2-3		0	3	H
2-4		0	4	H
2-5		0	5	MeO
2-6		S	1	H
2-7		O	1	MeO
2-8		O	1	Cl

Table 2 (cont.)









Compound No.	X	Y	m	R
2-9		O	1	Me
2-10		S	1	MeO
2-11		O	1	H
2-12		O	2	H
2-13		O	3	H
2-14		O	4	H
2-15		O	5	H
2-16		S	1	H

Table 2 (cont.)









Compound No.	X	Y	m	R
2-17		S	2	H
2-18		O	1	MeO
2-19		O	1	EtO
2-20		O	1	Cl
2-21		O	1	F
2-22		O	1	Me
2-23		O	1	<i>i</i> Pr
2-24		O	2	Et

Table 2 (cont.)









Compound No.	X	Y	m	R
2-25		S	1	Cl
2-26		S	1	Me
2-27		O	1	H
2-28		O	2	H
2-29		O	3	<i>t</i> Bu
2-30		O	1	Me
2-31		O	1	MeO
2-32		S	1	H

Table 2 (cont.)









Compound No.	X	Y	m	R
2-33		S	1	PrO
2-34		S	1	Me
2-35		O	1	H
2-36		O	3	H
2-37		O	1	F
2-38		S	1	H
2-39		O	1	H
2-40		O	2	H

Table 2 (cont.)

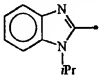
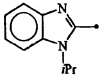
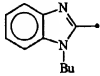
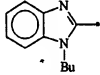
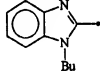
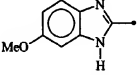
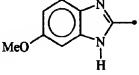
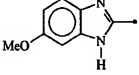
Compound No.	X	Y	m	R
2-41		S	1	H
2-42		S	5	Cl
2-43		O	1	H
2-44		O	4	H
2-45		S	1	H
2-46		O	1	H
2-47		O	3	H
2-48		S	1	H

Table 2 (cont.)

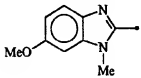
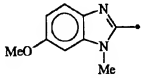
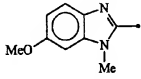
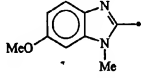
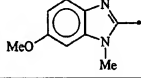
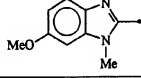
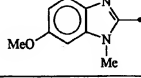
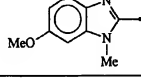
Compound No.	X	Y	m	R
2-49		O	1	H
2-50		O	2	H
2-51		O	3	H
2-52		O	4	H
2-53		O	5	H
2-54		S	1	H
2-55		S	2	H
2-56		O	1	Me

Table 2 (cont.)

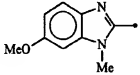
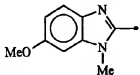
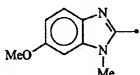
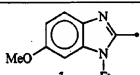
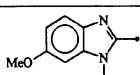
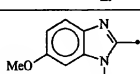
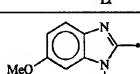
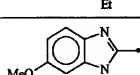
Compound No.	X	Y	m	R
2-57		O	1	MeO
2-58		O	1	F
2-59		O	1	Cl
2-60		O	1	H
2-61		O	2	H
2-62		O	1	MeO
2-63		S	1	H
2-64		O	1	H

Table 2 (cont.)

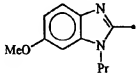
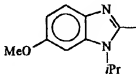
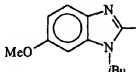
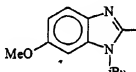
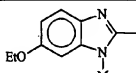
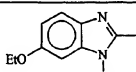
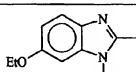
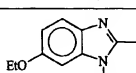
Compound No.	X	Y	m	R
2-65		S	1	H
2-66		O	1	H
2-67		O	1	H
2-68		S	1	H
2-69		O	1	H
2-70		O	1	MeO
2-71		O	1	Cl
2-72		O	2	H

Table 2 (cont.)

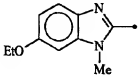
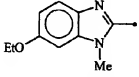
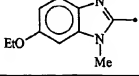
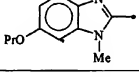
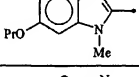
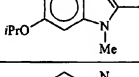
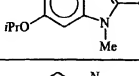
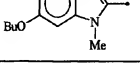
Compound No.	X	Y	m	R
2-73		O	3	H
2-74		S	1	H
2-75		S	4	Et
2-76		O	1	H
2-77		S	1	H
2-78		O	1	H
2-79		O	3	H
2-80		O	1	H

Table 2 (cont.)

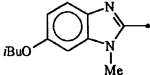
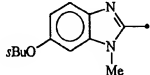
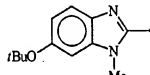
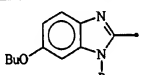
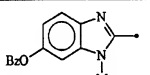
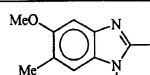
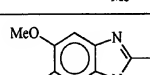
Compound No.	X	Y	m	R
2-81		O	1	H
2-82		O	1	H
2-83		O	1	H
2-84		O	1	H
2-85		O	1	H
2-86		O	1	H
2-87		O	1	H

Table 2 (cont.)

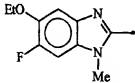
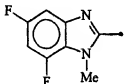
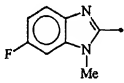
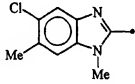
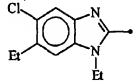
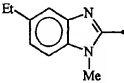
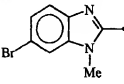
Compound No.	X	Y	m	R
2-88		O	1	H
2-89		O	1	H
2-90		O	1	H
2-91		O	1	H
2-92		O	1	H
2-93		O	1	H
2-94		O	1	H

Table 2 (cont.)

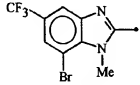
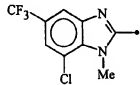

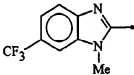
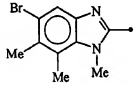
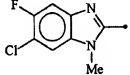
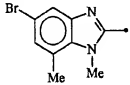
Compound No.	X	Y	m	R
2-95		O	1	H
2-96		O	1	H
2-97		O	1	H
2-98		O	1	H
2-99		O	1	H
2-100		O	1	H
2-101		O	1	H

Table 2 (cont.)

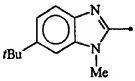
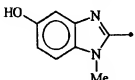
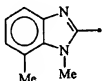
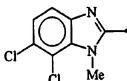
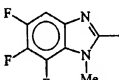
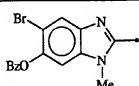
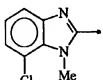
Compound No.	X	Y	m	R
2-102		O	1	H
2-103		O	1	H
2-104		O	1	H
2-105		O	1	H
2-106		O	1	H
2-107		O	1	H
2-108		O	1	H

Table 2 (cont.)

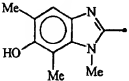
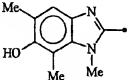
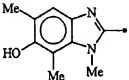
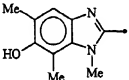
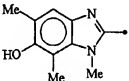
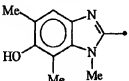
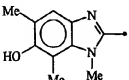
Compound No.	X	Y	m	R
2-109		O	1	H
2-110		O	2	H
2-111		O	3	H
2-112		S	1	H
2-113		O	1	Me
2-114		O	1	MeO
2-115		O	1	Cl

Table 2 (cont.)








Compound No.	X	Y	m	R
2-116		O	1	H
2-117		S	1	H
2-118		O	1	H
2-119		O	2	H
2-120		O	3	H
2-121		O	4	H
2-122		O	5	H

Table 2 (cont.)








Compound No.	X	Y	m	R
2-123		O	1	MeO
2-124		O	1	Cl
2-125		S	1	H
2-126		S	3	H
2-127		O	1	H
2-128		S	1	H
2-129		O	1	H

Table 2 (cont.)

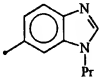
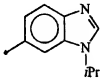
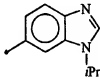
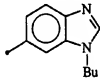
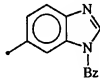
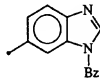
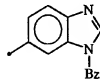
Compound No.	X	Y	m	R
2-130		O	1	Cl
2-131		O	1	H
2-132		S	1	H
2-133		O	1	H
2-134		O	1	H
2-135		O	3	H
2-136		S	1	H

Table 2 (cont.)








Compound No.	X	Y	m	R
2-137		O	1	H
2-138		O	1	H
2-139		O	1	H
2-140		S	1	H
2-141		O	1	H
2-142		O	1	H
2-143		O	1	H

Table 2 (cont.)

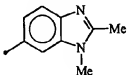
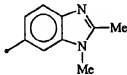
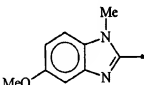
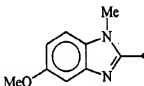
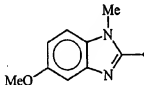
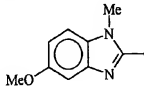
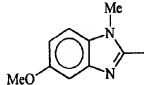
Compound No.	X	Y	m	R
2-144		O	1	H
2-145		S	1	H
2-146		O	1	H
2-147		O	2	H
2-148		O	3	H
2-149		O	4	H
2-150		O	5	H

Table 2 (cont.)

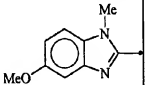
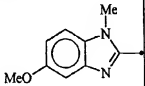
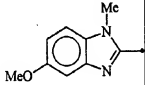
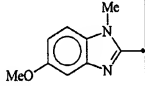
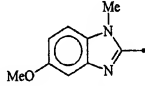
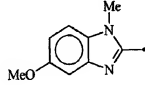
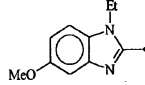
Compound No.	X	Y	m	R
2-151		S	1	H
2-152		S	2	H
2-153		O	1	Me
2-154		O	2	Me
2-155		O	1	F
2-156		O	1	Cl
2-157		O	1	H

Table 2 (cont.)

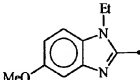
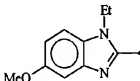
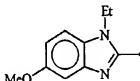
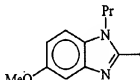
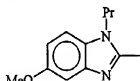
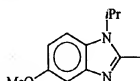
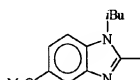
Compound No.	X	Y	m	R
2-158		O	2	H
2-159		O	1	MeO
2-160		S	1	H
2-161		O	1	H
2-162		S	1	H
2-163		O	1	H
2-164		O	1	H

Table 2 (cont.)

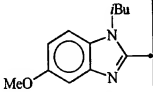
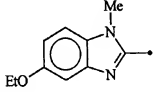
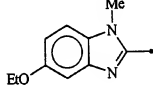
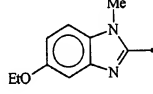
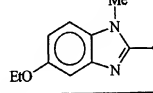
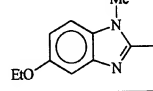
Compound No.	X	Y	m	R
2-165		S	1	H
2-166		O	1	H
2-167		O	1	MeO
2-168		O	1	Cl
2-169		O	2	H
2-170		O	3	H

Table 2 (cont.)

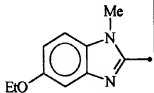
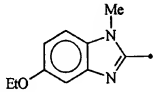
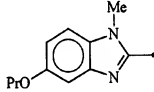
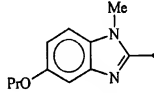
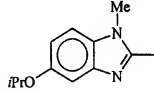
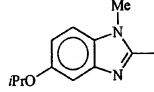
Compound No.	X	Y	m	R
2-171		S	1	H
2-172		S	4	Et
2-173		O	1	H
2-174		S	1	H
2-175		O	1	H
2-176		O	3	H

Table 2 (cont.)

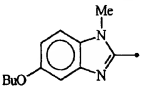
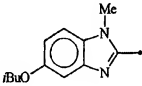
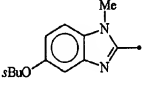
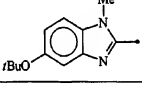
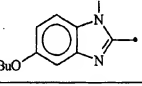
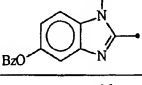
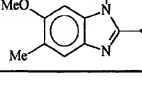
Compound No.	X	Y	m	R
2-177		O	1	H
2-178		O	1	H
2-179		O	1	H
2-180		O	1	H
2-181		O	1	H
2-182		O	1	H
2-183		O	1	H

Table 2 (cont.)

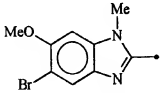
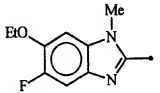
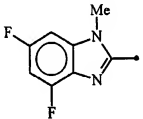
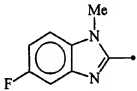
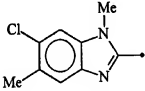
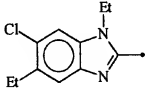
Compound No.	X	Y	m	R
2-184		O	1	H
2-185		O	1	H
2-186		O	1	H
2-187		O	1	H
2-188		O	1	H
2-189		O	1	H

Table 2 (cont.)

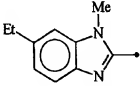
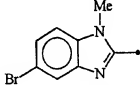
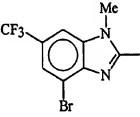
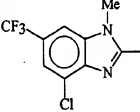
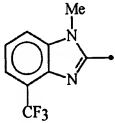
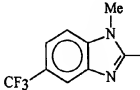
Compound No.	X	Y	m	R
2-190		O	1	H
2-191		O	1	H
2-192		O	1	H
2-193		O	1	H
2-194		O	1	H
2-195		O	1	H

Table 2 (cont.)

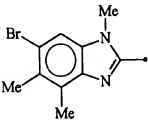
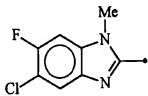
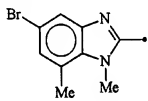
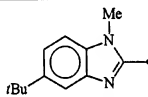
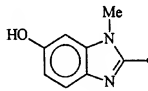
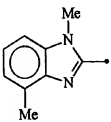
Compound No.	X	Y	m	R
2-196		O	1	H
2-197		O	1	H
2-198		O	2	H
2-199		O	1	H
2-200		O	1	H
2-201		O	1	H

Table 2 (cont.)

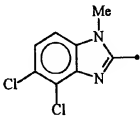
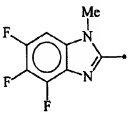
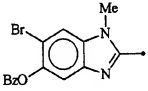
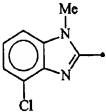
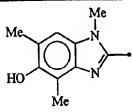
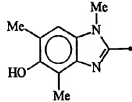
Compound No.	X	Y	m	R
2-202		O	1	H
2-203		O	1	H
2-204		O	1	H
2-205		O	1	H
2-206		O	1	H
2-207		O	2	H

Table 2 (cont.)

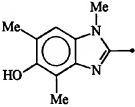
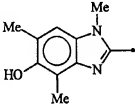
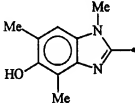
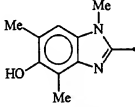
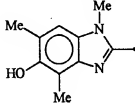

Compound No.	X	Y	m	R
2-208		O	3	H
2-209		S	1	H
2-210		O	1	Me
2-211		O	1	MeO
2-212		O	1	Cl
2-213		O	1	H

Table 2 (cont.)









Compound No.	X	Y	m	R
2-214		O	2	H
2-215		O	3	H
2-216		O	4	H
2-217		O	5	H
2-218		O	1	MeO
2-219		O	1	Cl
2-220		S	1	H
2-221		S	3	H

Table 2 (cont.)









Compound No.	X	Y	m	R
2-222		O	1	H
2-223		S	1	H
2-224		O	1	H
2-225		O	1	Cl
2-226		O	1	H
2-227		S	1	H
2-228		O	1	H
2-229		O	1	H

Table 2. (cont.)




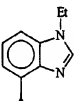
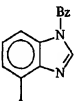
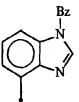
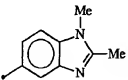
Compound No.	X	Y	m	R
2-230		O	3	H
2-231		S	1	H
2-232		O	1	H
2-233		O	1	H
2-234		O	1	H
2-235		S	1	H
2-236		O	1	H

Table 3









Compound No.	X	Y	m	R
3-1		0	1	H
3-2		0	2	H
3-3		0	3	H
3-4		0	4	H
3-5		0	5	MeO
3-6		S	1	H
3-7		O	1	MeO
3-8		O	1	Cl

Table 3 (cont.)









Compound No.	X	Y	m	R
3-9		O	1	Me
3-10		S	1	MeO
3-11		O	1	H
3-12		O	2	H
3-13		O	3	H
3-14		O	4	H
3-15		O	5	H
3-16		S	1	H

Table 3 (cont.)









Compound No.	X	Y	m	R
3-17		S	2	H
3-18		O	1	MeO
3-19		O	1	EtO
3-20		O	1	Cl
3-21		O	1	F
3-22		O	1	Me
3-23		O	1	<i>i</i> Pr
3-24		O	2	Et

Table 3 (cont.)









Compound No.	X	Y	m	R
3-25		S	1	Cl
3-26		S	1	Me
3-27		O	1	H
3-28		O	2	H
3-29		O	3	tBu
3-30		O	1	Me
3-31		O	1	MeO
3-32		S	1	H

Table 3 (cont.)








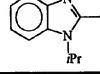
Compound No.	X	Y	m	R
3-33		S	1	PrO
3-34		S	1	Me
3-35		O	1	H
3-36		O	3	H
3-37		O	1	F
3-38		S	1	H
3-39		O	1	H
3-40		O	2	H

Table 3 (cont.)






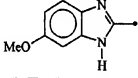
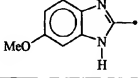
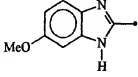
Compound No.	X	Y	m	R
3-41		S	1	H
3-42		S	5	Cl
3-43		O	1	H
3-44		O	4	H
3-45		S	1	H
3-46		O	1	H
3-47		O	3	H
3-48		S	1	H

Table 3 (cont.)

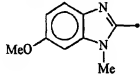
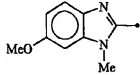
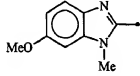
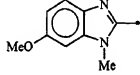
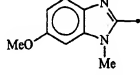
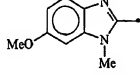
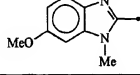
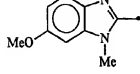
Compound No.	X	Y	m	R
3-49		O	1	H
3-50		O	2	H
3-51		O	3	H
3-52		O	4	H
3-53		O	5	H
3-54		S	1	H
3-55		S	2	H
3-56		O	1	Me

Table 3 (cont.)

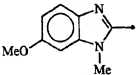
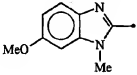
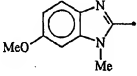
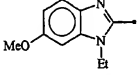
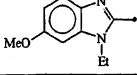
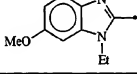
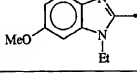
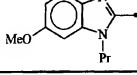
Compound No.	X	Y	m	R
3-57		O	1	MeO
3-58		O	1	F
3-59		O	1	Cl
3-60		O	1	H
3-61		O	2	H
3-62		O	1	MeO
3-63		S	1	H
3-64		O	1	H

Table 3 (cont.)

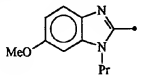
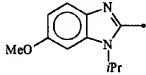
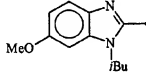
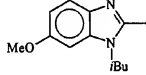
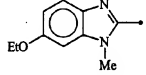
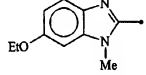
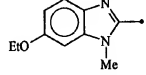
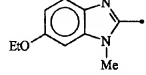
Compound No.	X	Y	m	R
3-65		S	1	H
3-66		O	1	H
3-67		O	1	H
3-68		S	1	H
3-69		O	1	H
3-70		O	1	MeO
3-71		O	1	Cl
3-72		O	2	H

Table 3 (cont.)

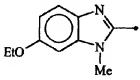
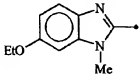
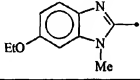
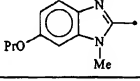
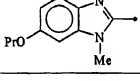
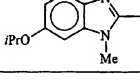
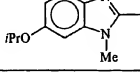
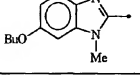
Compound No.	X	Y	m	R
3-73		O	3	H
3-74		S	1	H
3-75		S	4	Et
3-76		O	1	H
3-77		S	1	H
3-78		O	1	H
3-79		O	3	H
3-80		O	1	H

Table 3 (cont.)

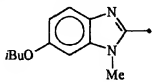
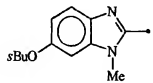
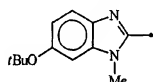
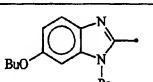
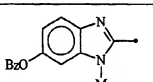
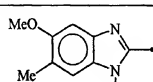
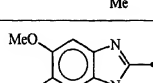
Compound No.	X	Y	m	R
3-81		O	1	H
3-82		O	1	H
3-83		O	1	H
3-84		O	1	H
3-85		O	1	H
3-86		O	1	H
3-87		O	1	H

Table 3 (cont.)

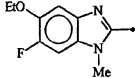
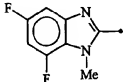
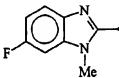
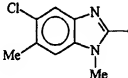
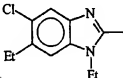
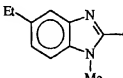
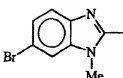
Compound No.	X	Y	m	R
3-88		O	1	H
3-89		O	1	H
3-90		O	1	H
3-91		O	1	H
3-92		O	1	H
3-93		O	1	H
3-94		O	1	H

Table 3 (cont.)

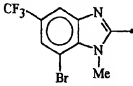
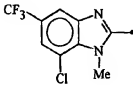

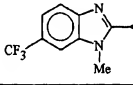
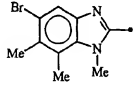
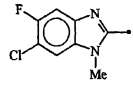
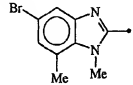
Compound No.	X	Y	m	R
3-95		O	1	H
3-96		O	1	H
3-97		O	1	H
3-98		O	1	H
3-99		O	1	H
3-100		O	1	H
3-101		O	1	H

Table 3 (cont.)

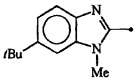
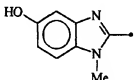
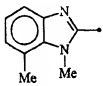
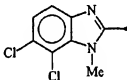
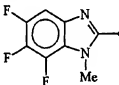
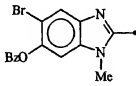

Compound No.	X	Y	m	R
3-102		O	1	H
3-103		O	1	H
3-104		O	1	H
3-105		O	1	H
3-106		O	1	H
3-107		O	1	H
3-108		O	1	H

Table 3 (cont.)

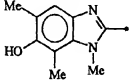
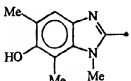
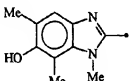
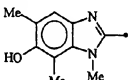
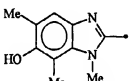
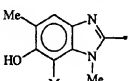
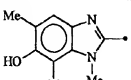
Compound No.	X	Y	m	R
3-109		O	1	H
3-110		O	2	H
3-111		O	3	H
3-112		S	1	H
3-113		O	1	Me
3-114		O	1	MeO
3-115		O	1	Cl

Table 3 (cont.)

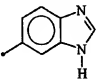
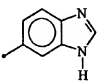
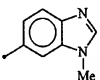
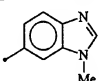
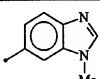
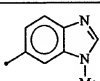
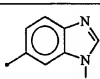
Compound No.	X	Y	m	R
3-116		O	1	H
3-117		S	1	H
3-118		O	1	H
3-119		O	2	H
3-120		O	3	H
3-121		O	4	H
3-122		O	5	H

Table 3 (cont.)

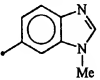
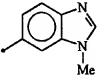
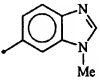
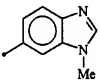
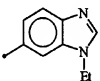
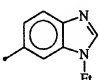
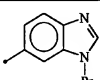
Compound No.	X	Y	m	R
3-123		O	1	MeO
3-124		O	1	Cl
3-125		S	1	H
3-126		S	3	H
3-127		O	1	H
3-128		S	1	H
3-129		O	1	H

Table 3 (cont.)

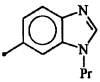
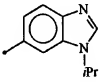
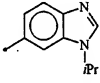
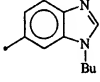
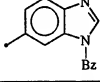
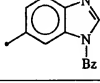

Compound No.	X	Y	m	R
3-130		O	1	Cl
3-131		O	1	H
3-132		S	1	H
3-133		O	1	H
3-134		O	1	H
3-135		O	3	H
3-136		S	1	H

Table 3 (cont.)








Compound No.	X	Y	m	R
3-137		O	1	H
3-138		O	1	H
3-139		O	1	H
3-140		S	1	H
3-141		O	1	H
3-142		O	1	H
3-143		O	1	H

Table 3 (cont.)

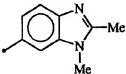
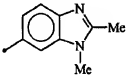
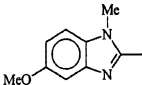
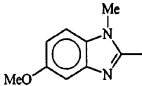
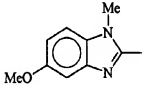
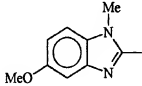
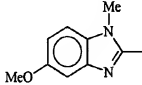
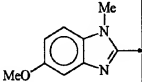
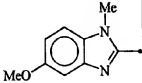
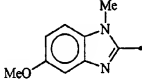
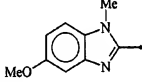
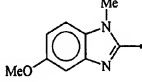
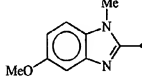
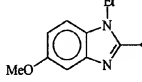
Compound No.	X	Y	m	R
3-144		O	1	H
3-145		S	1	H
3-146		O	1	H
3-147		O	2	H
3-148		O	3	H
3-149		O	4	H
3-150		O	5	H

Table 3 (cont.)

Compound No.	X	Y	m	R
3-151		S	1	H
3-152		S	2	H
3-153		O	1	Me
3-154		O	2	Me
3-155		O	1	F
3-156		O	1	Cl
3-157		O	1	H